

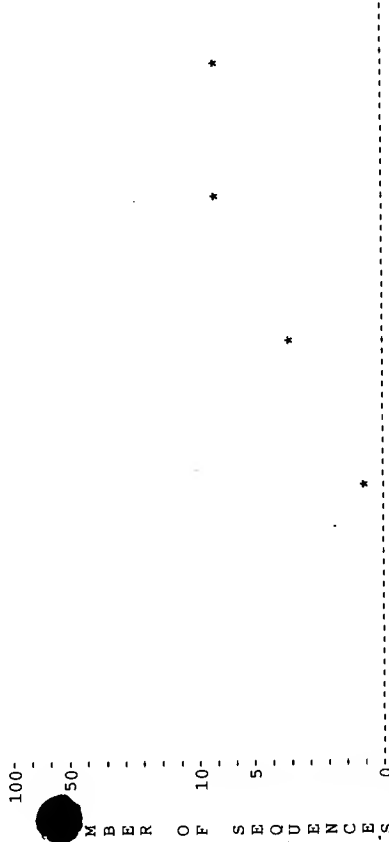
> O <  
> O < IntelliGenetics  
> O <

FastDB - Fast Pairwise Comparison of Sequences  
Release 5.4

Results file us-09-095-639a-1.res made by bobryen on Mon 3 Mar 103 11:47:56-PST.

Query sequence being compared: US-09-095-639A-1 (1-5)  
Number of sequences searched: 18  
Number of scores above cutoff: 18

Results of the initial comparison of US-09-095-639A-1 (1-5) with:  
File: betabovine.pep



Similarity matrix PAM-150 K-tuple 1  
Threshold level of sim. 16% PD 10-JUL-1997.  
Match penalty 1 Joining penalty 20  
Size penalty 5.00 Window size 5  
Cutoff score 0.05  
Randomization group 0

SEARCH STATISTICS

Scores: Mean 4 Median 5 Standard Deviation 0.90  
Times: CPU 00:00:00.00 Total Elapsed 00:00:00.00

Number of residues: 1156  
Number of sequences searched: 18  
Number of scores above cutoff: 18

The scores below are sorted by initial score.  
Significance is calculated based on initial score.  
2 100% identical sequences to the query sequence were found:

Sequence Name Description Length Score Init. Opt. Significance  
Residue Identity = 100% Matches = 5 Mismatches = 0

- 1. W31287 Bovine beta casein variant A1 5 5 5 1.11 0
  - 2. aaw31287 Bovine beta casein variant A1 5 5 5 1.11 0
- 5 100% similar sequences to the query sequence were found:

Sequence Name	Description	Length	Score	Init. Opt.	Sig. Frame
3. R95609	Bovine beta casein A1 variant	209	5	5	1.11 0
4. R80281	Methyl or ethyl esterified bo	209	5	5	1.11 0
5. aar95609	Bovine beta casein A1 variant	209	5	5	1.11 0
6. W31289	Bovine beta casein variant A1	12	5	5	1.11 0
7. aaw31289	Bovine beta casein variant A1	12	5	5	1.11 0

The list of other best scores is:

Sequence Name	Description	Length	Score	Init. Opt.	Sig. Frame
8. W31293	Bovine beta casein immunogeni	4	4	4	0.00 0
9. aaw31293	Bovine beta casein immunogeni	4	4	4	0.00 0
10. W31288	Bovine beta casein variant A2	5	4	4	0.00 0
11. aaw31288	Bovine beta casein variant A2	5	4	4	0.00 0
12. W31290	Bovine beta casein variant A2	12	4	4	0.00 0
13. aaw31290	Bovine beta casein variant A2	12	4	4	0.00 0
14. p02666	Beta casein precursor.	224	4	4	0.00 0
	**** 1 standard deviation below mean ****				
15. W31294	Bovine beta casein immunogeni	4	3	3	1.11 0
16. aaw31294	Bovine beta casein immunogeni	4	3	3	1.11 0
17. p02662	Alpha-S1 casein precursor.	214	3	3	1.11 0
	**** 2 standard deviations below mean ****				
18. R37103	Bovine milk beta-casein enzym	7	2	3	-2.22 0

- 1. US-09-095-639A-1 (1-5)  
W31287 Bovine beta casein variant A1 immunogenic peptide

ID W31287 standard; peptide; 5 AA.  
AC W31287;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A1 immunogenic peptide motif.  
KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-EM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PI (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 5; Page 3; 34pp; English.  
CC This sequence represents an immunogenic peptide motif from the A1  
CC variant of beta-casein which is capable of mimicking a fragment of the  
CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
CC a known correlation between exposure to cow's milk and the development of  
CC insulin-dependent diabetes which could possibly be linked to this  
CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
CC substantially free of non-human beta casein or containing modified  
CC beta-casein without this motif could be used in diets for the prevention  
CC of insulin dependent diabetes particularly during early infancy.  
SQ Sequence 5 AA:  
SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial score = 5 Optimized score = 5 Significance = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0

Gaps - 0 Conservative Substitutions - 0

X X  
PGPIH  
|||||  
PGPIH  
X X

2. US-09-095-639A-1 (1-5)  
aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide; 5 AA.

XX AAW31287;

AC  
XX  
DT 05-MAR-1998 (first entry)

XX Bovine beta casein variant A1 immunogenic peptide motif.

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX Bos taurus.

XX WO9724371-A1.

XX 10-JUL-1997.

XX 27-DEC-1996; 96WO-EP05846.

XX 27-DEC-1995; 95IT-OR08050.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.

XX Pozzilli P;

XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
XX food or pharmaceutical products for prevention of insulin dependent  
XX diabetes, particularly in early infancy

XX Claim 5; Page 3; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A1  
XX variant of beta-casein which is capable of mimicking a fragment of the  
XX GLUT2 protein found in insulin producing cells of the pancreas. There is  
XX a known correlation between exposure to cow's milk and the development of  
XX insulin-dependent diabetes which could possibly be linked to this  
XX molecular mimicry. Dietary or pharmaceutical products derived from milk  
XX substantially free of non-human beta casein or containing modified  
XX beta-casein without this motif could be used in diets for the prevention  
XX of insulin dependent diabetes particularly during early infancy.

XX Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114

Initial Score = 5 Optimized Score = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
X  
PGPIH  
|||||  
PGPIH  
X X

3. US-09-095-639A-1 (1-5)  
R95609 Bovine beta casein A1 variant.

ID R95609 standard; protein; 209 AA.

AC R95609;

DT 26-NOV-1996 (first entry)

DE Bovine beta casein A1 variant.

KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;

KW butter; cheese; cream.

OS Bos taurus.

FT Key

FT region

FT Location/Qualifiers

FT 63..68

FT /label= Diabetogenic hexapeptide.

PN WO9614577-A1.

PD 17-MAY-1996.

PF 03-NOV-1995; NZ0114.

PR 04-NOV-1994; NZ-264862.

PA (NACH-) NAT CHILD HEALTH RES FOUND.

PA (NZDA-) NEW ZEALAND DAIRY BOARD.

PI Elliott RB. Hill JP;

PI WPI; 96-251885/25.

PT Selecting non-diabetogenic milk and milk prods. - by testing milk or

PT cows for the presence of non-diabetogenic variants of beta-casein

PS Disclosure; Figure 2; 28pp; English.

CC A method for selecting milk for feeding to diabetes susceptible

CC individuals comprises testing milk from identified cows for the

CC presence of variants of beta casein and selecting those cows whose

CC milk contains non-diabetogenic variants and milking these cows

CC separately. The milk and milk products obtained can reduce the risk

CC of susceptible individuals contracting Type-1 diabetes.

CC Sequence 209 AA;

SQ 5 A; 4 R; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;

SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;

CC Retrieved by bobyren on Thu 27 Feb 103 16:22:05-PST using FindSeq

Initial Score = 5 Optimized Score = 5 Significance = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
X  
PGPIH  
|||||  
PGPIH  
X X

4. US-09-095-639A-1 (1-5)

R80281 Methyl or ethyl esterified bovine beta-casein A1.

ID R80281 standard; protein; 209 AA.

AC R80281;

DT 14-FEB-1996 (first entry)

DE Methyl or ethyl esterified bovine beta-casein A1.

KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;

KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.

OS Bos taurus.

FT Key

FT Location/Qualifiers

FT 1..209

FT /note= "55% esterified by methanol or by

FT ethanol, resulting in atypical pepsin

FT cleavage sites, in addition to the

FT naturally occurring (native) sites"

FT cleavage\_site

FT 4..5

FT /note= "pepsin cleavage site in native protein"

FT 5..6

FT /note= "pepsin cleavage site in native protein and

FT in methyl ester of beta-casein"

FT 11..12

FT /note= "newly identified pepsin cleavage site in

FT methyl ester of beta-casein"

FT 15..16

FT /note= "pepsin cleavage site in native protein"

FT 44..45

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FT FT /note= "pepsin cleavage site in native protein"
FT FT 45..46
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 55..56
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 57..58
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 58..59
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 72..73
FT FT /note= "pepsin cleavage site in native protein"
FT FT 73..74
FT FT /note= "newly identified pepsin cleavage site in
FT FT methyl ester of beta-casein"
FT FT 80..81
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 93..94
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl and ethyl esters of beta-casein"
FT FT 125..126
FT FT /note= "pepsin cleavage site in native protein"
FT FT 126..127
FT FT /note= "pepsin cleavage site in native protein"
FT FT 127..128
FT FT /note= "pepsin cleavage site in native protein"
FT FT 141..142
FT FT /note= "pepsin cleavage site in native protein"
FT FT 142..143
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl and ethyl esters of beta-casein"
FT FT 156..157
FT FT /note= "newly identified pepsin cleavage site in
FT FT ethyl ester of beta-casein"
FT FT 162..163
FT FT /note= "newly identified pepsin cleavage site in
FT FT ethyl ester of beta-casein"
FT FT 163..164
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl and ethyl esters of beta-casein"
FT FT 164..165
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 188..189
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl ester of beta-casein"
FT FT 189..190
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl and ethyl esters of beta-casein"
FT FT 190..191
FT FT /note= "pepsin cleavage site in native protein and
FT FT in ethyl ester of beta-casein"
FT FT 191..192
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl and ethyl esters of beta-casein"
FT FT 192..193
FT FT /note= "pepsin cleavage site in native protein and
FT FT in methyl and ethyl esters of beta-casein"
FT FT 198..199
FT FT /note= "newly identified pepsin cleavage site in
FT FT methyl and ethyl esters of beta-casein"
FT FT 207..208
FT FT /note= "newly identified pepsin cleavage site in
FT FT methyl ester of beta-casein"
FT FT 2..25
FT FT /label= A
FT FT /note= "tryptic peptide from native protein"
FT FT 26..28
FT FT /label= B
FT FT
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peptide
FT FT /note= "tryptic peptide from native protein"
FT FT 29..32
FT FT /label= C
FT FT /note= "tryptic peptide from native protein"
FT FT 33..48
FT FT /label= D
FT FT /note= "tryptic peptide from native protein"
FT FT 49..97
FT FT /label= E
FT FT /note= "tryptic peptide from native protein"
FT FT 100..105
FT FT /label= F
FT FT /note= "tryptic peptide from native protein"
FT FT 106..107
FT FT /label= G
FT FT /note= "tryptic peptide from native protein"
FT FT 108..113
FT FT /label= H
FT FT /note= "tryptic peptide from native protein"
FT FT 114..169
FT FT /label= I
FT FT /note= "tryptic peptide from native protein"
FT FT 170..176
FT FT /label= J
FT FT /note= "tryptic peptide from native protein"
FT FT 177..183
FT FT /label= K
FT FT /note= "tryptic peptide from native protein"
FT FT 184..202
FT FT /label= L
FT FT /note= "tryptic peptide from native protein"
FT FT 203..209
FT FT /label= N
FT FT /note= "tryptic peptide from native protein"
FT FT 15
FT FT /note= "phosphorylated"
FT FT 17
FT FT /note= "phosphorylated"
FT FT 18
FT FT /note= "phosphorylated"
FT FT 19
FT FT /note= "phosphorylated"
FT FT 35
FT FT /note= "phosphorylated"
FT FT
FT FT WQ9517518-Al.
FT FT 29-JUN-1995.
FT FT 20-DEC-1994; F01500.
FT FT 23-DEC-1993; FR-015764.
FT FT (INRG ) INST NAT RECH AGRONOMIQUE.
FT FT Briand L, Chobert J, Haertle T;
FT FT WPL; 95-240679/31.
FT FT New esterified amino acids, peptide(s) and their mixts, - prepd. by
FT FT esterification of protein then enzymatic hydrolysis, useful as
FT FT ingredients and additives in foods, pharmaceuticals and cosmetics
FT FT Claim 7; Fig 7 and 18; 47pp; French.
FT FT The native form of bovine beta-casein Al contains various pepsin
FT FT cleavage sites. Esterification of the protein with methanol or ethanol
FT FT results in a form of beta-casein contg. additional, non-conventional
FT FT pepsin cleavage sites (see Features Table). Esterified peptides and
FT FT amino acids (and their mixtures) resulting from hydrolysis of an
FT FT esterified protein (pref. beta-lactoglobulin or beta-casein) are
FT FT claimed. The hydrolysis products are useful as ingredients,
FT FT additives or active agents in foods, pharmaceuticals and cosmetics.
FT FT
FT FT Sequence 209 AA;
FT FT 5 A; 4 R; 5 N; 4 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;
FT FT 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;
FT FT Retrieved by bobryen on Thu 27 Feb 103 16:22:04 PST using FindSeq
FT FT
FT FT Initial score = 5 Optimized score = 5 Significance = 1.11
FT FT Residue identity = 100% Matches = 5 Mismatches = 0
FT FT Gaps = 0
FT FT
FT FT X X
```

PGPIH  
|||||  
AQTQSLVYPPFGPIHNSLPQNIPPL  
60 X X 70

5. US-09-095-639A-1 (1-5)  
aas95609 Bovine beta casein Al variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

ID AAR95609 standard; protein; 209 AA.

AC AAR95609;

DE 26-NOV-1996 (first entry)

DE Bovine beta casein Al variant.

KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
butter; cheese; cream.

OS Bos taurus.

PH Key Location/Qualifiers

FT Region 63. .68

FT /label= Diabetogenic hexapeptide.

XX WO9614577-A1.

XX 17-MAY-1996.

XX 03-NOV-1995; 95WO-NZ001114.

XX 04-NOV-1994; 94NZ-0264862.

XX (NACH-) NAT CHILD HEALTH RES FOUND.

XX (NZDA-) NEW ZEALAND DAIRY BOARD.

XX Elliott RB, Hill JP;

XX WPI; 1996-251885/25.

Selecting non-diabetogenic milk and milk prods. - by testing milk or  
cows for the presence of non-diabetogenic variants of beta-casein

PS Disclosure; Figure 2; 28pp; English.

CC A method for selecting milk for feeding to diabetes susceptible  
individuals comprises testing milk from identified cows for the  
presence of variants of beta casein and selecting those cows whose  
milk contains non-diabetogenic variants and milking these cows  
separately. The milk and milk products obtained can reduce the risk  
of susceptible individuals contracting Type-1 diabetes.

XX Sequence 209 AA;

AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014

Initial Score = 5 Optimized Score = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

XX X  
PGPIH  
|||||  
AQTQSLVYPPFGPIHNSLPQNIPPL  
60 X X 70

6. US-09-095-639A-1 (1-5)  
W31289 Bovine beta casein variant Al immunogenic peptide.

ID W31289 standard; peptide; 12 AA.  
AC W31289;  
DE 05-MAR-1998 (first entry)  
DE Bovine beta casein variant Al immunogenic peptide.  
KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
food or pharmaceutical products for prevention of insulin dependent  
diabetes, particularly in early infancy  
PS Claim 5; Page 3; 34pp; English.  
CC This sequence represents an immunogenic peptide from the Al variant of  
beta-casein which contains a motif (see W31287) capable of mimicking a  
fragment of the GLUT2 protein found in insulin producing cells of the  
pancreas. There is a known correlation between exposure to cow's milk and  
the development of insulin-dependent diabetes which could possibly be  
linked to this molecular mimicry. Dietary or pharmaceutical products  
derived from milk substantially free of non-human beta casein or  
containing modified beta-casein without this motif could be used in diets  
for the prevention of insulin dependent diabetes particularly during  
early infancy.

SQ Sequence 12 AA;

SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
Retrieved by bobryen on Thu 27 Feb 103 16:22:07 PST using FindSeq

Initial Score = 5 Optimized Score = 1.11  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

XX X  
PGPIH  
|||||  
SLVYPPFGPIH  
X 10

7. US-09-095-639A-1 (1-5)  
aaw31289 Bovine beta casein variant Al immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.

XX AAW31289;

XX 05-MAR-1998 (first entry)

DE Bovine beta casein variant Al immunogenic peptide.

KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

PN WO9724371-A1.

PD 10-JUL-1997.

XX 27-DEC-1996; 96WO-EP05846.

XX 27-DEC-1995; 95IT-ORM0850.

XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.

XX Pozzilli P;  
 XX WPI; 1997-363622/33.  
 XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 XX Claim 5; Page 3; 34pp; English.  
 XX This sequence represents an immunogenic peptide from the A1 variant of  
 CC beta-casein which contains a motif (see AAW31287) capable of mimicking a  
 CC fragment of the GLUT2 protein found in insulin producing cells of the  
 CC pancreas. There is a known correlation between exposure to cow's milk  
 CC and the development of insulin-dependent diabetes which could possibly  
 CC be linked to this molecular mimicry. Dietary or pharmaceutical products  
 CC derived from milk substantially free of non-human beta casein or  
 CC containing modified beta-casein without this motif could be used in  
 CC diets for the prevention of insulin dependent diabetes particularly  
 XX during early infancy.  
 XX SQ Sequence 12 AA;

AAW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975 ..  
 Initial Score = 5 Optimized Score = 1.11  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 X GPIH  
 ||||  
 SLVPPPGPIH  
 X 10

8. US-09-095-639A-1 (1-5)  
 W31293 Bovine beta casein immunogenic peptide motif 1.

ID W31293 standard; peptide; 4 AA.  
 AC W31293;  
 DT 05-MAR-1998 (first entry)  
 DE Bovine beta casein immunogenic peptide motif 1.  
 KW Beta casein; immunogenic; molecular mimicry; cow;  
 KW milk product; insulin-dependent diabetes; GLUT2; diet.  
 OS Bos taurus.  
 WO9724371-A1.  
 10-JUL-1997.  
 27-DEC-1996; E05846.  
 PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.  
 PI Pozzilli P;  
 DR WPI; 97-363622/33.  
 PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 PS Claim 10; Page 6; 34pp; English.  
 CC This sequence represents an immunogenic peptide motif of beta-casein  
 CC which is capable of mimicking a fragment of the GLUT2 protein found in  
 CC insulin producing cells of the pancreas. There is a known correlation  
 CC between exposure to cow's milk and the development of insulin-dependent  
 CC diabetes which could possibly be linked to this molecular mimicry.  
 CC Dietary or pharmaceutical products derived from milk substantially free  
 CC of non-human beta casein or containing modified beta-casein without this  
 CC motif could be used in diets for the prevention of insulin dependent  
 CC diabetes particularly during early infancy.  
 CC Sequence 4 AA;

SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 X GPIH  
 ||||  
 GPIH  
 X X

9. US-09-095-639A-1 (1-5)  
 aaw31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaw31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.

XX AC AAW31293;  
 XX DT 05-MAR-1998 (first entry)  
 XX DE Bovine beta casein immunogenic peptide motif 1.  
 XX KW Beta casein; immunogenic; molecular mimicry; cow;  
 KW milk product; insulin-dependent diabetes; GLUT2; diet.  
 OS Bos taurus.  
 XX WO9724371-A1.  
 XX PD 10-JUL-1997.  
 XX PF 27-DEC-1996; 96WO-EP05846.  
 XX PR 27-DEC-1995; 95IT-OR0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.

PI Pozzilli P;

XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy

XX Claim 10; Page 6; 34pp; English.

XX This sequence represents an immunogenic peptide motif of beta-casein  
 CC which is capable of mimicking a fragment of the GLUT2 protein found in  
 CC insulin producing cells of the pancreas. There is a known correlation  
 CC between exposure to cow's milk and the development of insulin-dependent  
 CC diabetes which could possibly be linked to this molecular mimicry.  
 CC Dietary or pharmaceutical products derived from milk substantially free  
 CC of non-human beta casein or containing modified beta-casein without this  
 CC motif could be used in diets for the prevention of insulin dependent  
 CC diabetes particularly during early infancy.

XX Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738 ..

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 X GPIH  
 ||||  
 GPIH  
 X X

10. US-09-095-639A-1 (1-5)  
W31288 Bovine beta casein variant A2 immunogenic peptide

ID W31288 standard; peptide; 5 AA.  
AC W31288;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A2 immunogenic peptide motif.  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
Claim 5; Page 4; 34pp; English.  
This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid position 63-68). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
PGPIP  
X X

11. US-09-095-639A-1 (1-5)  
aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5

AAW31288 standard; peptide; 5 AA.

ID AAW31288;  
AC AAW31288;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A2 immunogenic peptide motif.  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus  
PN WO9724371-A1.  
PD 10-JUL-1997.

XX 27-DEC-1996; 96WO-E05846.  
XX 27-DEC-1995; 95IT-ORM0850.  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.  
XX Pozzilli P;  
XX WPI; 1997-363622/33.  
XX Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
XX Claim 5; Page 4; 34pp; English.

This sequence represents an immunogenic peptide motif from the A2 variant beta-casein found in both Bos taurus and Bos indicus (amino acid position 63-68). This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
PGPIP  
X X

12. US-09-095-639A-1 (1-5)  
W31290 Bovine beta casein variant A2 immunogenic peptide.

ID W31290 standard; peptide; 12 AA.

AC W31290;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A2 immunogenic peptide.  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus.  
PN WO9724371-A1.  
PD 10-JUL-1997.

PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.

PI Pozzilli P;  
WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
Claim 5; Page 4; 34pp; English.  
This sequence represents an immunogenic peptide from the A2 variant of beta-casein found in both Bos taurus and Bos indicus. The peptide contains a motif (see W31288) corresponding to amino acids 63-68 of the A2 beta casein protein and is found to be capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the

CC development of insulin-dependent diabetes which could possibly be linked  
CC to this molecular mimicry. Dietary or pharmaceutical products derived  
CC from milk substantially free of non-human beta casein or containing  
CC modified beta-casein without this motif could be used in diets for the  
CC prevention of insulin dependent diabetes particularly during early  
CC infancy. 12 AA;  
SQ Sequence = 12 AA;  
SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobyron on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
SLVYPPFGPIP  
X 10

13. US-09-095-639A-1 (1-5)  
aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

ID AAW31290 standard; peptide; 12 AA.

AC AAW31290;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-MAR-1989 (Rel. 10, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Beta casein precursor.  
GN CSN2.  
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
RT "Primary structure of bovine beta casein CDNA.";  
RL Mol. Biol. (Mosk) 21:214-222(1987).  
RN [2]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=88188989; PubMed=2833669;  
RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
RA Mackinlay A.G.;  
RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
RT CDNAs: comparisons with related sequences in other species.";  
RL Mol. Biol. Evol. 4:231-241(1987).  
RN [3]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=90147279; PubMed=3271384;  
RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
RT "Complete nucleotide sequence of the bovine beta-casein gene.";  
RL Aust. J. Biol. Sci. 41:527-537(1988).  
RN [4]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=97128158; PubMed=3814153;  
RA Jimenez-Flores R., Kang Y.C., Richardson T.;  
RT "Cloning and sequence analysis of bovine beta-casein CDNA.";  
RL Biochem. Biophys. Res. Commun. 142:617-621(1987).  
RN [5]  
RP SEQUENCE FROM N.A. (VARIANT A3).  
RC TISSUE=Mammary gland;  
RX MEDLINE=94068382; PubMed=8248100;  
RA Simons G., van den Heuvel W., Reynen T., Frieters A., Rutten G.,  
RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
RT "Overproduction of bovine beta-casein in Escherichia coli and  
RT engineering of its main chymosin cleavage site.";  
RL protein Eng. 6:763-770(1993).  
RN [6]  
RP SEQUENCE OF 16-224 (VARIANT A2).  
RX MEDLINE=88152252; PubMed=3278933;  
RA Charles C., Huet J.-C., Ribadeau-Dumas B.;  
RT "A new strategy for primary structure determination of proteins:

CC early infancy.  
XX  
SQ Sequence 12 AA;

AW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..  
Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
SLVYPPFGPIP  
X 10

14. US-09-095-639A-1 (1-5)  
p02666 Beta casein precursor.

TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASB\_BOVIN STANDARD; PRT; 224 AA.  
AC P02666;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-MAR-1989 (Rel. 10, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Beta casein precursor.  
GN CSN2.

OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
RT "Primary structure of bovine beta casein CDNA.";  
RL Mol. Biol. (Mosk) 21:214-222(1987).  
RN [2]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=88188989; PubMed=2833669;  
RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
RA Mackinlay A.G.;  
RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
RT CDNAs: comparisons with related sequences in other species.";  
RL Mol. Biol. Evol. 4:231-241(1987).  
RN [3]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=90147279; PubMed=3271384;  
RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
RT "Complete nucleotide sequence of the bovine beta-casein gene.";  
RL Aust. J. Biol. Sci. 41:527-537(1988).  
RN [4]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=97128158; PubMed=3814153;  
RA Jimenez-Flores R., Kang Y.C., Richardson T.;  
RT "Cloning and sequence analysis of bovine beta-casein CDNA.";  
RL Biochem. Biophys. Res. Commun. 142:617-621(1987).  
RN [5]  
RP SEQUENCE FROM N.A. (VARIANT A3).  
RC TISSUE=Mammary gland;  
RX MEDLINE=94068382; PubMed=8248100;  
RA Simons G., van den Heuvel W., Reynen T., Frieters A., Rutten G.,  
RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
RT "Overproduction of bovine beta-casein in Escherichia coli and  
RT engineering of its main chymosin cleavage site.";  
RL protein Eng. 6:763-770(1993).  
RN [6]  
RP SEQUENCE OF 16-224 (VARIANT A2).  
RX MEDLINE=88152252; PubMed=3278933;  
RA Charles C., Huet J.-C., Ribadeau-Dumas B.;  
RT "A new strategy for primary structure determination of proteins:

RT application to bovine beta-casein.";  
RN FEBS Lett. 229:265-272(1988).  
RN [7]  
RP SEQUENCE OF 16-224 (VARIANT A2).  
RX MEDLINE=72233212; PubMed=4557764;  
RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;  
RT "Primary structure of bovine beta casein. Complete sequence.";  
RN Eur. J. Biochem. 25:505-514(1972).  
RN [8]  
RP VARIANTS A1; B AND C.  
RX MEDLINE=72214259; PubMed=5064450;  
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Characterization of genetic variants of alpha-S1 and beta bovine  
RN caseins.";  
RN Eur. J. Biochem. 26:328-337(1972).  
RN [9]  
RP SEQUENCE OF 118-124 (VARIANT A3).  
RX MEDLINE=71252171; PubMed=4997616;  
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
RT "Localization in the peptide chain of bovine beta casein of the  
RN His-cln substitution differentiating the A2 and A3 genetic  
RN variants.";  
RN C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
RN [10]  
RP SEQUENCE OF 48-63 (VARIANT E).  
RX MEDLINE=75005247; PubMed=4411121;  
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
RT "The beta E variant and the phosphorylation code of bovine caseins.";  
RN FEBS Lett. 45:3-5(1974).  
RN [11]  
RP SEQUENCE OF 68-105 FROM N.A.  
RX MEDLINE=85155504; PubMed=6397405;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Siliimova G.E., Judinkova E.S., Gorodetsky S.I.;  
RT "Identification of bacterial clones encoding bovine caseins by direct  
RN immunological screening of the cDNA library.";  
RN Gene 32:381-388(1984).  
RN [12]  
RP SEQUENCE OF 68-95 FROM N.A.  
RX MEDLINE=86014005; PubMed=3900695;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Siliimova G.E.;  
RT "Identification of bacterial clones coding for bovine caseins by  
RN direct immunologic screening of the cDNA library.";  
RN Mol. Biol. (Mosk) 19:955-963(1985).  
RN [13]  
RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE=20154951; PubMed=10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RN beta-casein variant detected in Korean cattle.";  
RN Anim. Genet. 31:49-51(2000).  
RN [14]  
RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RX Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RN casein by peptide mapping and mass spectrometric analysis.";  
RN Int. Dairy J. 8:967-972(1998).  
RN [15]  
RP SEQUENCE OF 160-171 (VARIANT F).  
RX MEDLINE=96118672; PubMed=7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RA Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RN reversed-phase high-performance liquid chromatography and mass  
RN spectrometric analysis.";  
RN J. Chromatogr. A 711:141-150(1995).  
RN [16]  
RP SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RN analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RN

DNA 1:375-386(1982).  
RN [17]  
RP CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wold F.;  
RT "Neoglycoproteins: in vitro introduction of glycosyl units at  
RN glutamines in beta-casein using transglutaminase.";  
RN Biochemistry 23:3759-3765(1984).  
RN [18]  
RP FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLE.  
CC -|- SUBCELLULAR LOCATION: Extracellular.  
CC -|- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -|- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190  
CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -|- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -|- DATABASE: NAME-Protein Spotlight;  
CC NOTE=Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptl016.html".  
CC -----  
CC THIS SWISS-PROT entry is copyright. It is produced through a collaboration  
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
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CC or send an email to license@isb-sib.ch).  
CC -----  
DR EMBL; M16645; AAA30480.1; -  
DR EMBL; M15132; AAA30430.1; -  
DR EMBL; K01087; AAA30481.1; -  
DR EMBL; X06359; CAA29658.1; -  
DR EMBL; M55158; AAA30431.1; -  
DR EMBL; S67277; AAB29137.1; -  
DR EMBL; AF104929; AAD09813.1; -  
DR EMBL; AF104928; AAD09813.1; JOINED.  
DR EMBL; M64756; AAB59254.1; -  
DR PIR; A03110; KBB0A2.  
DR PIR; A25846; A25846.  
DR PIR; B29087; B29087.  
DR PIR; S01860; S01860.  
DR PIR; S02429; S02429.  
DR Carlsberg; CCSD:9067; -  
DR InterPro; IPR001588; Casein.  
DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224  
FT MOD\_RES 30 30 BETA CASEIN.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION.  
FT CARBOHYD 70 70 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. .) (PARTIAL).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT VARIANT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVKPPPIIV -> DPSLLL (IN REF. 1).



SQ SEQUENCE 224 AA; 25107 MW; F0BBD8148A238AE CRC64;

P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
AQTSLVYFFPGPIPNLSLPQNPPL  
70 80 X 90

15. US-09-095-639A-1 (1-5)  
W31294 Bovine beta casein immunogenic peptide motif 2.

DE W31294 standard; peptide; 4 AA.  
W31294;  
05-MAR-1998 (first entry)  
Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN W09724371-AL.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilll P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.  
CC This sequence represents an immunogenic peptide motif found in bovine  
CC beta casein. This motif is capable of mimicking a fragment of the  
CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
CC a known correlation between exposure to cow's milk and the development of  
CC insulin-dependent diabetes which could possibly be linked to this  
CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
CC substantially free of non-human beta casein or containing modified  
CC beta-casein without this motif could be used in diets for the prevention  
CC of insulin dependent diabetes particularly during early infancy.  
SQ Sequence 4 AA;  
0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 3 Optimized Score = 3 Significance = -1.11  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
GPIP  
X X

16. US-09-095-639A-1 (1-5)  
aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.  
XX  
AC AAW31294;  
XX  
DT 05-MAR-1998 (first entry)  
XX

DE Bovine beta casein immunogenic peptide motif 2.  
XX  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX  
OS Bos taurus.  
XX  
PN W09724371-AL.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
PR 27-DEC-1995; 95IT-ORM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilll P; \

WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

SQ Sequence 4 AA;

AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

Initial Score = 3 Optimized Score = 3 Significance = -1.11  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIH  
||||  
GPIP  
X X

17. US-09-095-639A-1 (1-5)  
p02662 Alpha-S1 casein precursor.

TOIG of: p02662 check: 2471 from: 1 to: 214

ID CAS1\_BOVIN STANDARD; PRT; 214 AA.  
AC P02662; Q28048;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-NOV-1990 (Rel. 16, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Alpha-S1 casein precursor.  
GN CSNIS1.

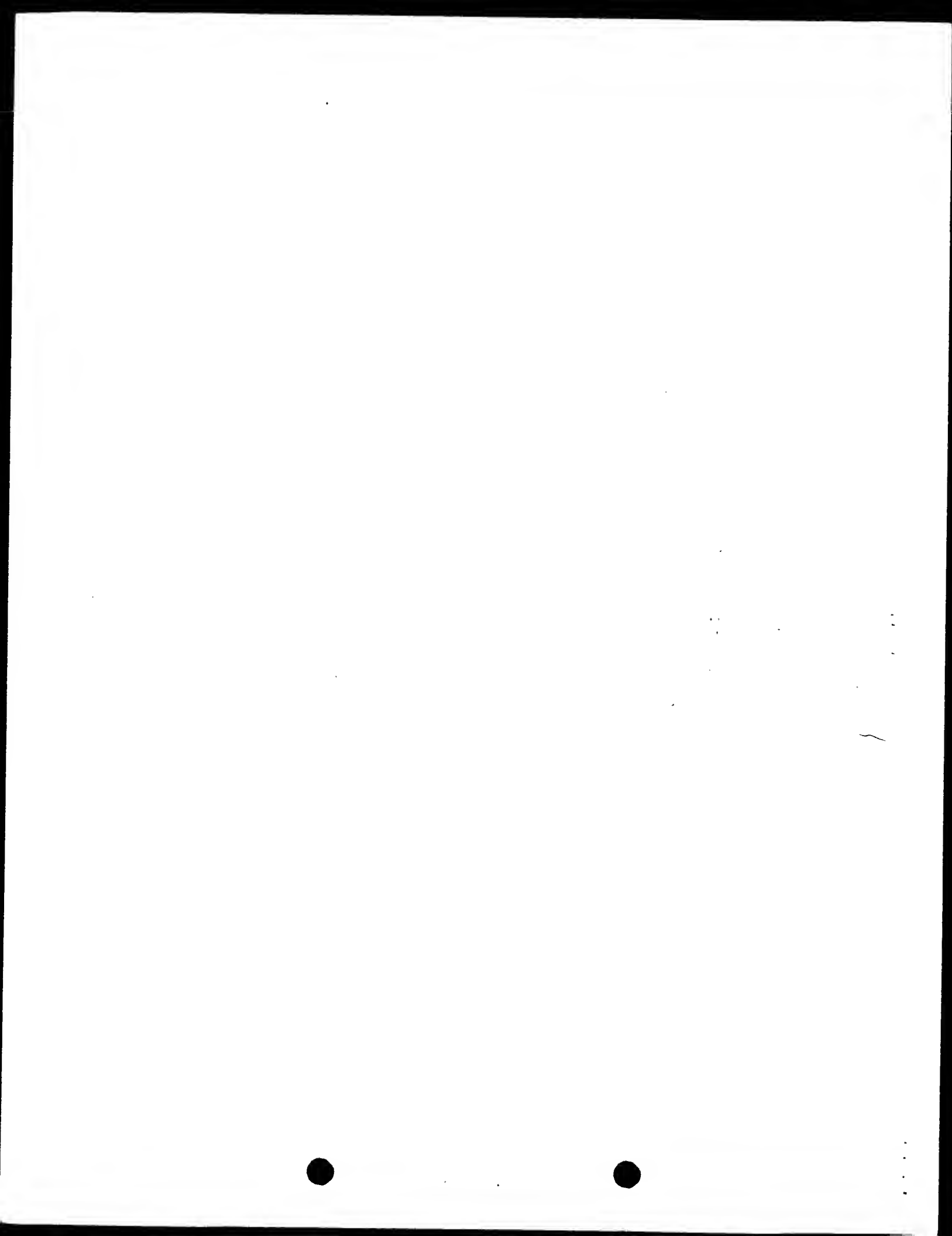
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=84221403; PubMed=6328443;



X X  
PGFIH  
| |  
YTDAPSFSDIPNPIGSENSEKTMPT  
190 200 X 210

18. US-09-095-639A-1 (1-5)  
R37103 Bovine milk beta-casein enzymatic fragment.  
ID R37103 standard; peptide; 7 AA.  
AC R37103;  
DT 21-MAY-1995 (first entry)  
DE Bovine milk beta-casein enzymatic fragment.  
KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
wrinkles.  
OS Bos Taurus.  
PN J06166615-A.  
PD 14-JUN-1994.  
01-DEC-1992; 321624.  
01-DEC-1992; JP-321624.  
(POKK ) POLA CHEM IND INC.  
DR WPI; 94-230615/28.  
PT Cosmetics for treating skin disorders and wrinkles - containing  
enzymatic hydrolysate of human or bovine milk beta-casein  
Claim 2; page 2; 7pp; Japanese.  
PS The invention relates to cosmetics containing human or bovine milk  
beta-casein enzymatic hydrolysate. The cosmetics are used for  
improving skin disorders and/or wrinkles. They are more effective  
than previously used polysaccharides, sugar alcohols, glycerol,  
glycols, etc.  
CC The present sequence is one component of the bovine milk beta-casein  
enzymatic hydrolysate.  
SQ Sequence 7 AA;  
SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
SQ 0 I; 0 L; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq  
Initial Score = 2 Optimized Score = 3 Significance = -2.22  
Residue Identity = 40% Matches = 2 Mismatches = 3  
Gaps = 0 Conservative Substitutions = 0

X X  
PGFIH  
| |  
AVPFPOR  
X X





Initial Score = 5 Optimized Score = 5 Significance = 1.19  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
|||||  
PGPIP  
X X

2. US-09-095-639A-2 (1-5)  
aaw31288 Bovine beta casein variant A2 immunogenic peptide  
TOIG of: aaw31288 check: 1154 from: 1 to: 5  
AAW31288 standard; peptide; 5 AA.

ID AAW31288;  
AC AAW31288;  
DT 05-MAR-1998 (first entry)  
Bovine beta casein variant A2 immunogenic peptide motif.

KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus  
XX W09724371-AL.  
XX 10-JUL-1997.

XX 27-DEC-1996; 96WO-EF05846.  
XX 27-DEC-1995; 95IT-OR0850.  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.

XX Pozzilli P;  
XX WPI; 1997-363622/33.  
XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
XX food or pharmaceutical products for prevention of insulin dependent  
XX diabetes, particularly in early infancy

XX Claim 5; Page 4; 34pp; English.  
XX This sequence represents an immunogenic peptide motif from the A2 variant  
XX beta-casein found in both Bos taurus and Bos indicus (amino acid  
XX position 63-68). This motif is capable of mimicking a fragment of the  
XX GLUT2 protein found in insulin producing cells of the pancreas. There is  
XX a known correlation between exposure to cow's milk and the development of  
XX insulin-dependent diabetes which could possibly be linked to this  
XX molecular mimicry. Dietary or pharmaceutical products derived from milk  
XX substantially free of non-human beta casein or containing modified  
XX beta-casein without this motif could be used in diets for the prevention  
XX of insulin dependent diabetes particularly during early infancy.

XX Sequence 5 AA;  
XX AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154

Initial Score = 5 Optimized Score = 5 Significance = 1.19  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
|||||

PGPIP  
X X

3. US-09-095-639A-2 (1-5)  
p02666 Beta casein precursor.  
TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASB\_BOVIN STANDARD; PRT; 224 AA.  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-MAR-1989 (Rel. 10, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Beta casein precursor.  
GN CSN2.  
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
RT "Primary structure of bovine beta-casein cDNA.";  
RL Mol. Biol. (Mosk) 21:214-222(1987).  
RN [2]  
RP SEQUENCE FROM N.A.  
RA MEDLINE=8818899; PubMed=2833669;  
RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
RA Mackinlay A.G.;  
RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
RT cDNAs: comparisons with related sequences in other species.";  
RL Mol. Biol. Evol. 4:231-241(1987).  
RN [3]  
RP SEQUENCE FROM N.A.  
RA MEDLINE=90147279; PubMed=3271384;  
RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
RT "Complete nucleotide sequence of the bovine beta-casein gene.";  
RL Aust. J. Biol. Sci. 41:527-537(1988).  
RN [4]  
RP SEQUENCE FROM N.A.  
RA MEDLINE=87128158; PubMed=3814153;  
RA Jimenez-Flores R., Kang Y.C., Richardson T.;  
RT "Cloning and sequence analysis of bovine beta-casein cDNA.";  
RL Biochem. Biophys. Res. Commun. 142:617-621(1987).  
RN [5]  
RP SEQUENCE FROM N.A. (VARIANT A3).  
RC TISSUE=Mammary gland;  
RX MEDLINE=94068382; PubMed=8248100;  
RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,  
RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
RT "Overproduction of bovine beta-casein in Escherichia coli and  
RT engineering of its main chymosin cleavage site.";  
RL protein Eng. 6:763-770(1993).  
RN [6]  
RP SEQUENCE OF 16-224 (VARIANT A2).  
RX MEDLINE=88152252; PubMed=3278933;  
RA Carles C., Huot J.-C., Ribadeau-Dumas B.;  
RT "A new strategy for primary structure determination of proteins:  
RT application to bovine beta-casein.";  
RL FEBS Lett. 229:265-272(1988).  
RN [7]  
RP SEQUENCE OF 16-224 (VARIANT A2).  
RX MEDLINE=7233212; PubMed=4557764;  
RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;  
RT "Primary structure of bovine beta casein. Complete sequence.";  
RL Eur. J. Biochem. 25:505-514(1978).  
RN [8]  
RP VARIANTS A1; B AND C.  
RX MEDLINE=72214259; PubMed=5064450;  
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Characterization of genetic variants of alpha-S1 and beta bovine

RT caseins.";  
RL Eur. J. Biochem. 26:328-337(1972).  
RN [9]  
RP SEQUENCE OF 118-124 (VARIANT A3).  
RX MEDLINE=71252171; PubMed=4997616;  
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
RT "Localization in the peptide chain of bovine beta casein of the  
RT His-Gln substitution differentiating the A2 and A3 genetic  
RT variants.";  
RL C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
RN [10]  
RP SEQUENCE OF 48-63 (VARIANT E).  
RX MEDLINE=75005247; PubMed=4411121;  
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
RT "The beta E variant and the phosphorylation code of bovine caseins.";  
RL FEBS Lett. 45:3-5(1974).  
RN [11]  
RP SEQUENCE OF 68-105 FROM N.A.  
RX MEDLINE=85155504; PubMed=6397405;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RT sulimova G.E., Judinkova E.S., Gordetsky S.I.;  
RT "Identification of bacterial clones encoding bovine caseins by direct  
RT immunological screening of the cDNA library.";  
RL Gene 32:381-388(1984).  
RN [12]  
RP SEQUENCE OF 68-95 FROM N.A.  
RX MEDLINE=85014005; PubMed=3900695;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RT Siliimova G.E.;  
RT "Identification of bacterial clones coding for bovine caseins by  
RT direct immunologic screening of the cDNA library.";  
RL Mol. Biol. (Mosk) 19:955-963(1985).  
RN [13]  
RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE=20154951; PubMed=10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RT beta-casein variant detected in Korean cattle.";  
RL Anim. Genet. 31:49-51(2000).  
RN [14]  
RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RX Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RT casein by peptide mapping and mass spectrometric analysis.";  
RL Int. Dairy J. 8:967-972(1998).  
RN [15]  
RP SEQUENCE OF 160-171 (VARIANT F).  
RX MEDLINE=96118672; PubMed=7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RT Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RT reversed-phase high-performance liquid chromatography and mass  
RT spectrometric analysis.";  
RL J. Chromatogr. A 711:141-150(1995).  
RN [16]  
RP SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RT analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RL DNA 1:375-386(1982).  
RN [17]  
RP CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wolf F.;  
RT "Neoglycoproteins: in vitro introduction of glycosyl units at  
RT glutamines in beta-casein using transglutaminase.";  
RL Biochemistry 23:3759-3765(1984).  
CC -1- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLES.  
CC -1- SUBCELLULAR LOCATION: Extracellular.  
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -1- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190

CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -1- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -1- DATABASE: NAME-Protein Spotlight;  
CC NOTE-Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptl016.html".  
CC  
CC THIS SWISS-PROT entry is copyright. It is produced through a collaboration  
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CC or send an email to license@isb-sib.ch).  
CC  
CC EMBL; M16645; AAA30480.1; -  
DR EMBL; M15132; AAA30430.1; -  
DR EMBL; K01087; AAA30481.1; -  
DR EMBL; X06359; CAA29658.1; -  
DR EMBL; M55158; AAA30431.1; -  
DR EMBL; S67277; AAB29137.1; -  
DR EMBL; AF104929; AAD09813.1; -  
DR EMBL; AF104928; AAD09813.1; JOINED.  
DR EMBL; M64756; AAB59254.1; -  
DR PIR; A03110; KBB0A2.  
DR PIR; A25846; A25846.  
DR PIR; B29087; B29087.  
DR PIR; S01860; S01860.  
DR PIR; S02429; S02429.  
DR Carlsbank; CCSD:9067; -  
DR InterPro; IPR001588; Casein.  
DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224  
FT MOD\_RES 30 30 BETA CASEIN  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. . .) (PARTIAL).  
FT CARBOHYD 70 70 O-LINKED (GALNAC. . .).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. . .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. . .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVRGPPPIIV -> DPSLLI (IN REF. 1).  
SQ SEQUENCE 224 AA; 25107 MW; F0BDD8148A238AE CRC64;  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
Initial Score = 5 Optimized Score = 5 Significance = 1.19  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
|||||  
AQTQSLVYFPFGPIPNLPQNPPL  
70 80 X 90

4. US-09-095-639A-2 (1-5)  
aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

ID AAW31290 standard; peptide; 12 AA.  
XX  
AC AAW31290;  
XX  
XX  
DT 05-MAR-1998 (first entry)  
XX  
DE Bovine beta casein variant A2 immunogenic peptide.  
XX  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
XX  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos indicus.  
XX  
PN W09724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 1997-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
KW food or pharmaceutical products for prevention of insulin dependent  
XX milk product; insulin-dependent diabetes; GLUT2; diet.  
XX  
OS Bos taurus.  
OS Bos indicus.

W09724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
XX 27-DEC-1995; 95IT-ORM0850.  
PR  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
XX Pozzilli P;  
XX  
XX WPI; 1997-363622/33.  
DR  
XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
XX food or pharmaceutical products for prevention of insulin dependent  
XX diabetes, particularly in early infancy  
XX  
XX Claim 5; Page 4; 34pp; English.

This sequence represents an immunogenic peptide from the A2 variant of  
beta-casein found in both Bos taurus and Bos indicus. The peptide  
contains a motif (see AAW31288) corresponding to amino acids 63-68 of  
the A2 beta casein protein and is found to be capable of mimicking a  
fragment of the GLUT2 protein found in insulin producing cells of the  
pancreas. There is a known correlation between exposure to cow's milk and  
the development of insulin-dependent diabetes which could possibly be  
linked to this molecular mimicry. Dietary or pharmaceutical products  
derived from milk substantially free of non-human beta casein or  
containing modified beta-casein without this motif could be used in diets  
for the prevention of insulin dependent diabetes particularly during  
early infancy.

XX Sequence 12 AA;

AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063 ..  
Initial Score = 5 Optimized Score = 5 Significance = 1.19  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions

XX X  
X  
PGPIP  
|||||  
SLVYPPGPIP  
X 10

5. US-09-095-639A-2 (1-5)  
W31290 Bovine beta casein variant A2 immunogenic peptide.

ID W31290 standard; peptide; 12 AA.  
AC W31290;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A2 immunogenic peptide.  
KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
OS Bos indicus.  
PN W09724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 5; Page 4; 34pp; English.  
CC This sequence represents an immunogenic peptide from the A2 variant of  
CC beta-casein found in both Bos taurus and Bos indicus. The peptide  
CC contains a motif (see W31288) corresponding to amino acids 63-68 of the  
CC A2 beta casein protein and is found to be capable of mimicking a fragment  
CC of the GLUT2 protein found in insulin producing cells of the pancreas.  
CC There is a known correlation between exposure to cow's milk and the  
CC development of insulin-dependent diabetes which could possibly be linked  
CC to this molecular mimicry. Dietary or pharmaceutical products derived  
CC from milk substantially free of non-human beta casein or containing  
CC modified beta-casein without this motif could be used in diets for the  
CC prevention of insulin dependent diabetes particularly during early  
CC infancy.  
SQ Sequence 12 AA;  
SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-FST using FindSeq  
Initial Score = 5 Optimized Score = 5 Significance = 1.19  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions

XX X  
X  
PGPIP  
|||||  
SLVYPPGPIP  
X 10

6. US-09-095-639A-2 (1-5)  
W31294 Bovine beta casein immunogenic peptide motif 2.

ID W31294 standard; peptide; 4 AA.  
AC W31294;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN W09724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif found in bovine  
beta casein. This motif is capable of mimicking a fragment of the  
GLUT2 protein found in insulin producing cells of the pancreas. There is



CC a known correlation between exposure to cow's milk and the development of  
 CC insulin-dependent diabetes which could possibly be linked to this  
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.  
 SQ Sequence 4 AA;  
 SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIP  
 ||||  
 GPII  
 X X

7. US-09-095-639A-2 (1-5)  
 aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.

XX AC AAW31294;

XX DT

XX 05-MAR-1998 (first entry)

XX DE Bovine beta casein immunogenic peptide motif 2.

XX KW Beta-casein; immunogenic; molecular mimicry; cow;

XX KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX PN WO9724371-AL.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-ORM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PI (MIDI-) MIDIA LTD.

XX PP Pozzilli P;

XX DR WPI; 1997-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 XX PT food or pharmaceutical products for prevention of insulin dependent  
 XX PT diabetes, particularly in early infancy

XX PS Claim 10; Page 6; 34pp; English.

XX CC This sequence represents an immunogenic peptide motif found in bovine  
 XX CC beta casein. This motif is capable of mimicking a fragment of the  
 XX CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
 XX CC a known correlation between exposure to cow's milk and the development of  
 XX CC insulin-dependent diabetes which could possibly be linked to this  
 XX CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 XX CC substantially free of non-human beta casein or containing modified  
 XX CC beta-casein without this motif could be used in diets for the prevention  
 XX CC of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 4 AA;

AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..  
 Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 100% Matches = 4 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIP  
 ||||  
 GPII  
 X X

8. US-09-095-639A-2 (1-5)  
 W31287 Bovine beta casein variant A1 immunogenic peptide

ID W31287 standard; peptide; 5 AA.

XX AC W31287;

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A1 immunogenic peptide motif.

XX KW A1 variant beta casein; immunogenic; molecular mimicry; cow;

XX KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX PN WO9724371-AL.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; E05846.

XX PR 27-DEC-1995; IT-RM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PI (MIDI-) MIDIA LTD.

XX PP Pozzilli P;

XX DR WPI; 97-363622/33.

XX PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 XX PT food or pharmaceutical products for prevention of insulin dependent  
 XX PT diabetes, particularly in early infancy

XX PS Claim 5; Page 3; 34pp; English.

XX CC This sequence represents an immunogenic peptide motif from the A1  
 XX CC variant of beta-casein which is capable of mimicking a fragment of the  
 XX CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
 XX CC a known correlation between exposure to cow's milk and the development of  
 XX CC insulin-dependent diabetes which could possibly be linked to this  
 XX CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 XX CC substantially free of non-human beta casein or containing modified  
 XX CC beta-casein without this motif could be used in diets for the prevention  
 XX CC of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 5 AA;

XX SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
 XX SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;

XX CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
 Residue Identity = 80% Matches = 4 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X X  
 PGPIP  
 ||||  
 GPII  
 X X

9. US-09-095-639A-2 (1-5)  
 aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide; 5 AA.

XX AC AAW31287;

XX DT 05-MAR-1998 (first entry)

XX DE Bovine beta casein variant A1 immunogenic peptide motif.

CC This sequence represents an immunogenic peptide from the A1 variant of  
CC beta-casein which contains a motif (see W31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk and  
CC the development of insulin-dependent diabetes which could possibly be  
CC linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in diets  
CC for the prevention of insulin dependent diabetes particularly during  
CC early infancy.  
SQ Sequence 12 AA;  
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
X  
PGPIP  
||||  
SLVYPPFGPIHN  
X 10

11. US-09-095-639A-2 (1-5)  
aaw31289 Bovine beta casein variant A1 immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.  
XX  
AC AAW31289;  
XX  
DT .05-MAR-1998 (first entry)  
XX  
DE Bovine beta casein variant A1 immunogenic peptide.  
XX  
KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
XX  
FN W09724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
PR 27-DEC-1995; 95IT-ORM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilli P;  
XX  
DR WPI; 1997-363622/33.  
XX  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 5; Page 3; 34pp; English.  
XX  
CC This sequence represents an immunogenic peptide from the A1 variant of  
CC beta-casein which contains a motif (see AAW31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk  
CC and the development of insulin-dependent diabetes which could possibly  
CC be linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in  
CC diets containing modified beta-casein without this motif could be used in

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX  
OS Bos taurus.  
XX  
PN W09724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
PR 27-DEC-1995; 95IT-ORM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilli P;  
XX  
DR WPI; 1997-363622/33.  
XX  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 5; Page 3; 34pp; English.

Initial Score = 4 Optimized Score = 4 Significance = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
X  
PGPIP  
||||  
PGPIH  
X X

10. US-09-095-639A-2 (1-5)  
W31289 Bovine beta casein variant A1 immunogenic peptide.

ID W31289 standard; peptide; 12 AA.  
AC W31289;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A1 immunogenic peptide.  
KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
XX  
PN W09724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; E05846.  
XX  
PR 27-DEC-1995; IT-RM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilli P;  
XX  
DR WPI; 97-363622/33.  
XX  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 5; Page 3; 34pp; English.

CC diets for the prevention of insulin dependent diabetes particularly during early infancy.

1

Sequence	12 AA:
S0	

```

AW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975 ..
Initial Score = 4 Optimized Score = 4 Significance = 0.00
Residue Identity = 80% Matches = 4 Mismatches = 1
Gaps = 0 Conservative Substitutions = 0

```

X X  
PGPIP  
||||  
SLVYPFPGPIHN  
X 10

US-09-095-639A-2 (1-5)  
R95609 Bovine beta casein A1 variant.

R95609 standard; protein; 209 AA.

R95609;

26-NOV-1996 (first entry)

Bovine beta casein Al variant.

Milk; beta casein; diabetogeni

butter; cheese: cream.

**Bos taurus.**

Key	Location/Qualifiers
100	100
101	101
102	102
103	103
104	104
105	105
106	106
107	107
108	108
109	109
110	110
111	111
112	112
113	113
114	114
115	115
116	116
117	117
118	118
119	119
120	120
121	121
122	122
123	123
124	124
125	125
126	126
127	127
128	128
129	129
130	130
131	131
132	132
133	133
134	134
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137	137
138	138
139	139
140	140
141	141
142	142
143	143
144	144
145	145
146	146
147	147
148	148
149	149
150	150
151	151
152	152
153	153
154	154
155	155
156	156
157	157
158	158
159	159
160	160
161	161
162	162
163	163
164	164
165	165
166	166
167	167
168	168
169	169
170	170
171	171
172	172
173	173
174	174
175	175
176	176
177	177
178	178
179	179
180	180
181	181
182	182
183	183
184	184
185	185
186	186
187	187
188	188
189	189
190	190
191	191
192	192
193	193
194	194
195	195
196	196
197	197
198	198
199	199

region

```

region:
  label = Diabetogenic environment
  00:00

```

WO9614577-A1

NO 2014577 AT,  
17-MAY-1996

03-NOV-1995. N7011A

03 NOV 1993, NZDT14.  
04-NOV-1994: N7-264963

04 NOV-1994; NZ-204862.  
(NACH-) NAT CHILD HEATHEN DEC FORN

(NACH-) NAT CHILD HEAR

(NZDA-) NEW ZEALAND  
Elliott RD 1111

ELLIOTT RB, HILL JP;  
WWT: 05-251005 '07

WPT; 96-251885/25.

selecting non-diabetogenic milk and

cows for the presence of non-diabetogenic variants of beta-casein

Disclosure; Figure 2; 28pp; English.

## A method for selecting milk for feeding to diabetes susceptible

Individuals comprises testing milk from identified cows for the

presence of variants of beta casein and selecting those cows whose

milk contains non-diabetogenic variants and milking these cows

separately. The m.

of susceptible individuals contracting Type-1 diabetes.

Sequence 209 AA;

5 A; 4 R; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;

10 I: 22 L; 11 K; 6 M; 9 F: 34 P: 16 S; 9 T; 1 W; 4 Y; 19 V;  
SQ  
CC Retrieved by bobryon on Thu 27 Feb 103 16:22:05-PSR using FindSeq

X X  
 PGPI  
 ||||  
 AQTQSLVYFP  
 60 X X

13. US-09-095-639A-2 (1-5)  
R80281 Methyl or ethyl esterified bovine beta-casein A1

P80281 extended: protocol: 200 22

K80261 standard; protein; 2  
P80381.

K80281;  
1A-FEB-1006 (first entry)

14-FEB-1996 (first entry)

Methyl or ethyl esterified bovine beta-casein Al.

Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;



SQ Sequence 209 AA;

AAR5609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014  
Initial Score = 4 Optimized Score = 0.00  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
||||  
AQTQSLVYFPFGPIHNSLPONIPPL  
60 X X 70

15. US-09-095-639A-2 (1-5)  
W31293 Bovine beta casein immunogenic peptide motif 1.

W31293 standard; peptide; 4 AA.

DE 05-MAR-1998 (first entry)  
KW Bovine beta casein immunogenic peptide motif 1.  
KW Beta casein; immunogenic; molecular mimicry; cow;  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN W09724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; II-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
FA (MIDI-) MIDIA LTD.  
PI Pozzilll P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.  
CC This sequence represents an immunogenic peptide motif of beta-casein  
CC which is capable of mimicking a fragment of the GLUT2 protein found in  
CC insulin producing cells of the pancreas. There is a known correlation  
CC between exposure to cow's milk and the development of insulin-dependent  
CC diabetes which could possibly be linked to this molecular mimicry.  
CC Dietary or pharmaceutical products derived from milk substantially free  
CC of non-human beta casein or containing modified beta-casein without this  
CC motif could be used in diets for the prevention of insulin dependent  
CC diabetes particularly during early infancy.  
SQ Sequence 4 AA;

Initial Score = 3 Optimized Score = 3 Significance = -1.19  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
X X  
PGPIP  
||||  
GPIH  
X X  
Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;

Initial Score = 3 Optimized Score = 3 Significance = -1.19  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
||||  
GPIH  
X X

16. US-09-095-639A-2 (1-5)  
aaw31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaw31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.  
XX  
AC AAW31293;  
XX  
DT 05-MAR-1998 (first entry)  
XX

DE Bovine beta casein immunogenic peptide motif 1.  
XX  
KW Beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX  
OS Bos taurus.  
XX  
PN W09724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
PR 27-DEC-1995; 95IT-ORM0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilll P;  
XX  
DR WPI; 1997-363622/33.  
XX  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 10; Page 6; 34pp; English.  
XX  
CC This sequence represents an immunogenic peptide motif of beta-casein  
CC which is capable of mimicking a fragment of the GLUT2 protein found in  
CC insulin producing cells of the pancreas. There is a known correlation  
CC between exposure to cow's milk and the development of insulin-dependent  
CC diabetes which could possibly be linked to this molecular mimicry.  
CC Dietary or pharmaceutical products derived from milk substantially free  
CC of non-human beta casein or containing modified beta-casein without this  
CC motif could be used in diets for the prevention of insulin dependent  
CC diabetes particularly during early infancy.  
XX  
SQ Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738  
Initial Score = 3 Optimized Score = 3 Significance = -1.19  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
X X  
PGPIP  
||||  
GPIH  
X X

17. US-09-095-639A-2 (1-5)  
p02662 Alpha-SI casein precursor.

TOIG of: p02662 check: 2471 from: 1 to: 214

ID CASI\_BOVIN STANDARD; PRT; 214 AA.  
AC P02662; 028048;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-NOV-1990 (Rel. 16, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Alpha-SI casein precursor.  
GN CSNLSI.  
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=84221403; PubMed=6328443;

RA Stewart A.F., Willis I.M., Mackinlay A.G.;  
 RT "Nucleotide sequences of bovine alpha S1- and kappa-casein cDNAs.";  
 RL Nucleic Acids Res. 12:3895-3907(1984).  
 RN [2]  
 RA SEQUENCE FROM N.A.  
 RP Naqao M., Maki M., Sasaki R., Chiba R.;  
 RT "Isolation and sequence analysis of bovine alpha-S1-casein cDNA  
 clone.";  
 RL Agric. Biol. Chem. 48:1663-1667(1984).  
 RN [3]  
 RA SEQUENCE FROM N.A.  
 RP MEDLINE=87049835; PubMed=3022833;  
 RX Gorodetskii S.I., Zakhar'ev V.M., Kyarshulite D.R., Kapelinskaya T.V.,  
 RA Skryabin K.G.;  
 RT "cDNA of cattle alpha S1-casein: cloning and nucleotide sequence.";  
 RL Biochimica 51:1641-1648(1986).  
 RN [4]  
 RA SEQUENCE FROM N.A.  
 RP MEDLINE=92051301; PubMed=1658736;  
 RX Kozzan D., Hobom G., Seyfert H.M.;  
 RA "Genomic organization of the bovine alpha-S1 casein gene.";  
 RL Nucleic Acids Res. 19:5591-5596(1991).  
 RN [5]  
 RA SEQUENCE OF 55-130 FROM N.A.  
 RP MEDLINE=83182023; PubMed=6897774;  
 RX Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
 RA "Construction and identification by partial nucleotide sequence  
 analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
 RL DNA 1:375-386(1982).  
 RN [6]  
 RA SEQUENCE OF 122-214 FROM N.A.  
 RP MEDLINE=85178933; PubMed=3838718;  
 RX Kiarshulite D.R., Zakhar'ev V.M., Gorodetskii S.I.;  
 RA "Nucleotide sequence of the 3'-nontranslated region of the mRNA of  
 alpha S1-casein in cows.";  
 RL Dokl. Akad. Nauk SSSR 280:1433-1437(1985).  
 RN [7]  
 RA SEQUENCE OF 164-214 FROM N.A.  
 RP MEDLINE=94154154; PubMed=1343827;  
 RX Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;  
 RA "Cloning, mapping, and sequencing of 3' and its flanking region of  
 bovine alpha-S1 casein gene.";  
 RL Chin. J. Biotechnol. 8:235-245(1992).  
 RN [8]  
 RA SEQUENCE OF 16-214 (VARIANT B).  
 RP MEDLINE=72063417; PubMed=4331376;  
 RX Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
 RA "Primary structure of bovine alpha-S1 casein. Complete sequence.";  
 RL Eur. J. Biochem. 23:41-51(1971).  
 RN [9]  
 RA REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).  
 RP MEDLINE=74082545; PubMed=4797901;  
 RX Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
 RA "Primary structure of alpha casein and of bovine beta casein.  
 Correction.";  
 RL Eur. J. Biochem. 40:323-323(1973).  
 RN [10]  
 RA SEQUENCE (VARIANT D).  
 RP MEDLINE=72214259; PubMed=5064450;  
 RX Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RA "Characterization of genetic variants of alpha-S1 and beta bovine  
 caseins.";  
 RL Eur. J. Biochem. 26:328-337(1972).  
 RN [11]  
 RA SEQUENCE OF 23-49 (VARIANT A).  
 RP Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RT "Localization in the N-terminal part of bovine casein alpha-S1 of a  
 13 amino-acid deletion that differentiates variant A from variants B  
 and C.";  
 RL FEBS Lett. 11:109-112(1970).  
 RN [12]  
 RA SEQUENCE OF 205-214 (VARIANT C).  
 RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;

RT On the localization in the C-terminal sequence of bovine casein  
 alpha-S1 of a Glu/Gly substitution that differentiates the genetic  
 variants B and C.;  
 RL C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).  
 RN [13]  
 RA REVISION (VARIANT C).  
 RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
 RL C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).  
 CC -1- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT  
 CALCIUM PHOSPHATE.  
 CC -1- SUBCELLULAR LOCATION: Extracellular.  
 CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
 CC -1- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.  
 CC -1- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.  
 CC -1- DATABASE: NAME=worthington enzyme manual;  
 WWW="http://www.worthington-biochem.com/manual/C/CASA.html".  
 CC -1- DATABASE: NAME=Protein Spotlight;  
 NOTE=Issue 16 of November 2001;  
 WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 between the Swiss Institute of Bioinformatics and the EMBL Outstation  
 the European Bioinformatics Institute. There are no restrictions on its  
 use by non-profit institutions as long as its content is in no way  
 modified and this statement is not removed. Usage by and for commercial  
 entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; X05564; CAB57792.1; -;  
 DR EMBL; M33123; AAA30428.1; -;  
 DR EMBL; M38641; AAA30429.1; -;  
 DR EMBL; X59856; CAA42516.1; -;  
 DR EMBL; K01084; AAA30478.1; -;  
 DR EMBL; M38658; AAA62707.1; -;  
 DR EMBL; S72388; AAD14099.1; -;  
 DR PIR; A03106; KABOSB.  
 DR PIR; A23071; A23071.  
 DR PIR; S02202; S02202.  
 DR PIR; S22575; S22575.  
 DR InterPro; IPR001586; Casein.  
 DR Pfam; PF00363; caseins; 1.  
 DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
 KW Milk; Phosphorylation; Signal; Repeat.  
 FT SIGNAL 1 15  
 FT CHAIN 16 214 ALPHA-S1 CASEIN.  
 FT MOD\_RES 61 61 PHOSPHORYLATION.  
 FT MOD\_RES 63 63 PHOSPHORYLATION.  
 FT MOD\_RES 68 68 PHOSPHORYLATION (IN VARIANT D).  
 FT MOD\_RES 79 79 PHOSPHORYLATION.  
 FT MOD\_RES 81 81 PHOSPHORYLATION.  
 FT MOD\_RES 82 82 PHOSPHORYLATION.  
 FT MOD\_RES 83 83 PHOSPHORYLATION.  
 FT MOD\_RES 90 90 PHOSPHORYLATION.  
 FT MOD\_RES 130 130 PHOSPHORYLATION.  
 FT REPEAT 85 99  
 FT REPEAT 125 140  
 FT REPEAT 29 41  
 FT VARIANT 68 68  
 FT VARIANT 207 207  
 FT VARIANT 42 42  
 FT CONFLICT 50 50  
 FT CONFLICT 95 95  
 FT CONFLICT 143 143  
 FT CONFLICT 203 203  
 FT CONFLICT 211 212  
 FT CONFLICT 214 214  
 FT SEQUENCE 214 AA; 24529 MW; F066B5C8AE55828B CRC64;  
 SQ  
 P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..  
 Initial Score = 3 Optimized Score = 4 Significance = -1.19  
 Residue Identity = 60% Matches = 3 Mismatches = 2  
 Caps = 0 Conservative Substitutions = 0

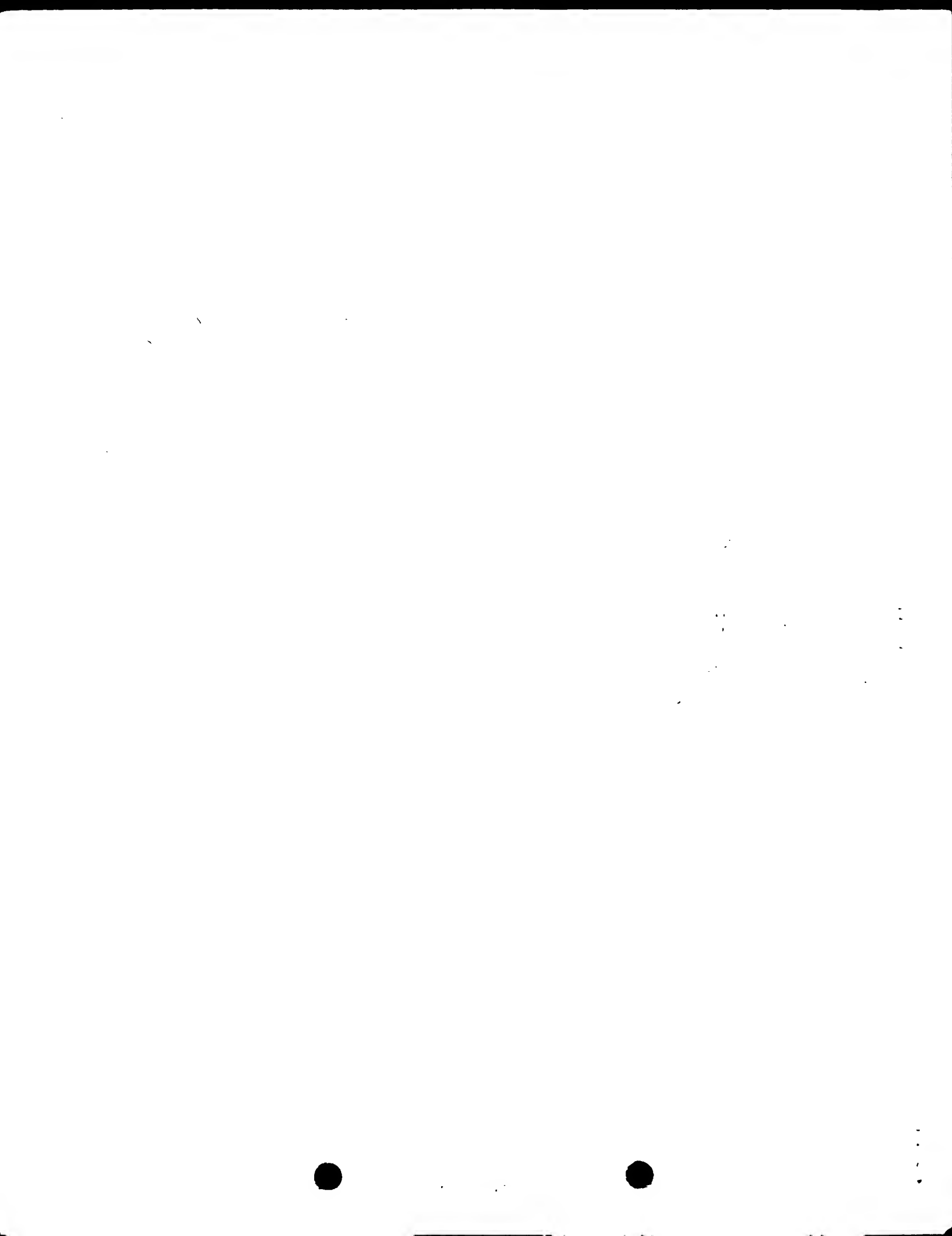
X X  
PGPIP  
| |  
YTDAPSFSDIPNPIGSENSEKTTMP  
190 200 X 210

18. US-09-095-639A-2 (1-5)  
R37103 Bovine milk beta-casein enzymatic fragment.

ID R37103 standard; peptide; 7 AA.  
AC R37103;  
DT 21-MAY-1995 (first entry)  
DE Bovine milk beta-casein enzymatic fragment.  
KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
KW wrinkles.  
OS Bos Taurus.  
PN J06166615-A.  
PD 14-JUN-1994.  
01-DEC-1992; 321624.  
01-DEC-1992; JP-321624.  
PA (POKK ) POLA CHEM IND INC.  
DR WPI; 94-230615/28.  
PT Cosmetics for treating skin disorders and wrinkles - containing  
PT enzymatic hydrolysate of human or bovine milk beta-casein  
PS Claim 2; Page 2; 7pp; Japanese.  
CC The invention relates to cosmetics containing human or bovine milk  
CC beta-casein enzymatic hydrolysate. The cosmetics are used for  
CC improving skin disorders and/or wrinkles. They are more effective  
CC than previously used polysaccharides, sugar alcohols, glycerol,  
CC glycols, etc.  
CC The present sequence is one component of the bovine milk beta-casein  
CC enzymatic hydrolysate.  
SQ Sequence 7 AA;  
SQ 1 A; 1 R; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
SQ 0 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq

Initial Score = 2 Optimized Score = 3 Significance = -2.38  
Residue Identity = 40% Matches = 2 Mismatches = 3  
Gaps = 0 Conservative Substitutions = 0

X X  
PGPIP  
| |  
AVPYEQR  
X X







Initial Score = 12 Optimized Score = 1.29  
Residue Identity = 100% Matches = 12 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIHN  
|||||  
SLVYPPFGPIHN  
X 10 X

2. US-09-095-639A-3 (1-12)  
aaw31289 Bovine beta casein variant Al immunogenic peptide.  
TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.  
AC AAW31289;  
XX  
XX 05-MAR-1998 (first entry)  
DE Bovine beta casein variant Al immunogenic peptide.  
KW Al variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; insulin-dependent diabetes; GLUT2; diet.  
XX Bos taurus.  
XX  
XX W09724371-AL.  
XX PD 10-JUL-1997.  
XX PF 27-DEC-1996; 96WO-EP05846.  
XX PR 27-DEC-1995; 95IT-ORM0850.  
XX  
XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
XX (MIDI-) MIDIA LTD.  
XX  
XX Pozzillini P;  
XX WPI; 1997-363622/33.  
XX  
XX beta-casein or fragments not showing mimicry with GLUT2 - used in  
XX food or pharmaceutical products for prevention of insulin dependent  
XX diabetes, particularly in early infancy  
XX  
XX Claim 5; Page 3; 34pp; English.

This sequence represents an immunogenic peptide from the Al variant of  
beta-casein which contains a motif (see AAW31287) capable of mimicking a  
fragment of the GLUT2 protein found in insulin producing cells of the  
pancreas. There is a known correlation between exposure to cow's milk  
and the development of insulin-dependent diabetes which could possibly  
be linked to this molecular mimicry. Dietary or pharmaceutical products  
derived from milk substantially free of non-human beta casein or  
containing modified beta-casein without this motif could be used in  
diets for the prevention of insulin dependent diabetes particularly  
during early infancy.

Sequence 12 AA;

AAW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975

Initial Score = 12 Optimized Score = 1.29  
Residue Identity = 100% Matches = 12 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIHN  
|||||  
SLVYPPFGPIHN

X 10 X

3. US-09-095-639A-3 (1-12)  
R95609 Bovine beta casein Al variant.

ID R95609 standard; protein; 209 AA.  
AC R95609;  
DE 26-NOV-1996 (first entry)  
DE Bovine beta casein Al variant.  
KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
KW butter; cheese; cream.  
OS Bos taurus.  
FH Key Location/Qualifiers  
FT region 63..68  
FT /label- Diabetogenic hexapeptide.

PN W09614577-AL.  
PD 17-MAY-1996.  
PF 03-NOV-1995; NZ0114.  
PR 04-NOV-1994; NZ-264862.  
PA (NACH-) NAT CHILD HEALTH RES FOUND.  
PA (NZDA-) NEW ZEALAND DAIRY BOARD.  
PI Elliott RB, Hill JP;  
DR WPI; 96-251885/25.  
PT Selecting non-diabetogenic milk and milk prods. - by testing milk or  
PT cows for the presence of non-diabetogenic variants of beta-casein  
PT A method for selecting milk for feeding to diabetes susceptible  
CC individuals comprises testing milk from identified cows for the  
CC presence of variants of beta casein and selecting those cows whose  
CC milk contains non-diabetogenic variants and milking these cows  
CC separately. The milk and milk products obtained can reduce the risk  
CC of susceptible individuals contracting Type-1 diabetes.  
SQ Sequence 209 AA;  
SQ 5 A; 4 R; 4 N; 5 D; 0 B; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;  
SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:05-PST using FindSeq

Initial Score = 12 Optimized Score = 1.29  
Residue Identity = 100% Matches = 12 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIHN  
|||||  
DKTHPPAQTSLVYPPFGPIHNSLPQNPPLT  
50 X 60 70

4. US-09-095-639A-3 (1-12)  
R80281 Methyl or ethyl esterified bovine beta-casein Al.

ID R80281 standard; protein; 209 AA.  
AC R80281;  
DE 14-FEB-1996 (first entry)  
DE Methyl or ethyl esterified bovine beta-casein Al.  
KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;  
KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.  
OS Bos taurus.  
FH Key Location/Qualifiers  
FT protein 1..209  
FT /note- "55% esterified by methanol or by  
FT ethanol, resulting in atypical pepsin  
FT cleavage sites, in addition to the  
FT naturally occurring (native) sites"  
FT cleavage\_site 4..5  
FT /note- "pepsin cleavage site in native protein"  
FT cleavage\_site 5..6  
FT /note- "pepsin cleavage site in native protein and  
FT in methyl ester of beta-casein"  
FT 11..12  
FT /note- "newly identified pepsin cleavage site in  
FT methyl ester of beta-casein"

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FT cleavage_site 15..16 /note= "pepsin cleavage site in native protein"
FT /label= B
FT cleavage_site 44..45 /note= "pepsin cleavage site in native protein"
FT /label= C
FT cleavage_site 45..46 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 55..56 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 57..58 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 58..59 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 72..73 /note= "pepsin cleavage site in native protein"
FT /label= G
FT cleavage_site 73..74 /note= "newly identified pepsin cleavage site in
FT methyl ester of beta-casein"
FT cleavage_site 80..81 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 93..94 /note= "pepsin cleavage site in native protein and
FT in methyl and ethyl esters of beta-casein"
FT cleavage_site 125..126 /note= "pepsin cleavage site in native protein"
FT /label= H
FT cleavage_site 126..127 /note= "pepsin cleavage site in native protein"
FT /label= I
FT cleavage_site 127..128 /note= "pepsin cleavage site in native protein"
FT /label= J
FT cleavage_site 141..142 /note= "pepsin cleavage site in native protein"
FT /label= K
FT cleavage_site 142..143 /note= "pepsin cleavage site in native protein"
FT /label= L
FT cleavage_site 156..157 /note= "pepsin cleavage site in native protein and
FT in methyl and ethyl esters of beta-casein"
FT cleavage_site 162..163 /note= "newly identified pepsin cleavage site in
FT ethyl ester of beta-casein"
FT cleavage_site 163..164 /note= "newly identified pepsin cleavage site in
FT in methyl and ethyl esters of beta-casein"
FT cleavage_site 164..165 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 188..189 /note= "pepsin cleavage site in native protein and
FT in methyl ester of beta-casein"
FT cleavage_site 189..190 /note= "pepsin cleavage site in native protein and
FT in methyl ester of beta-casein"
FT cleavage_site 190..191 /note= "pepsin cleavage site in native protein and
FT in ethyl ester of beta-casein"
FT cleavage_site 191..192 /note= "pepsin cleavage site in native protein and
FT in methyl and ethyl esters of beta-casein"
FT cleavage_site 192..193 /note= "pepsin cleavage site in native protein and
FT in methyl and ethyl esters of beta-casein"
FT cleavage_site 198..199 /note= "newly identified pepsin cleavage site in
FT methyl and ethyl esters of beta-casein"
FT cleavage_site 207..208 /note= "newly identified pepsin cleavage site in
FT methyl and ethyl esters of beta-casein"
FT peptide 2..25 /label= A
FT /note= "tryptic peptide from native protein"
FT 26..28 /label= B
FT /note= "tryptic peptide from native protein"
FT 29..32 /label= C
FT /note= "tryptic peptide from native protein"
FT 33..48 /label= D
FT /note= "tryptic peptide from native protein"
FT 49..97 /label= E
FT /note= "tryptic peptide from native protein"
FT 100..105 /label= F
FT /note= "tryptic peptide from native protein"
FT 106..107 /label= G
FT /note= "tryptic peptide from native protein"
FT 108..113 /label= H
FT /note= "tryptic peptide from native protein"
FT 114..169 /label= I
FT /note= "tryptic peptide from native protein"
FT 177..183 /label= J
FT /note= "tryptic peptide from native protein"
FT 184..202 /label= K
FT /note= "tryptic peptide from native protein"
FT 203..209 /label= L
FT /note= "tryptic peptide from native protein"
FT 15 /label= N
FT /note= "tryptic peptide from native protein"
FT 17 /note= "phosphorylated"
FT 18 /note= "phosphorylated"
FT 19 /note= "phosphorylated"
FT 35 /note= "phosphorylated"
FT /label= N
FT 15 /note= "tryptic peptide from native protein"
FT 17 /note= "phosphorylated"
FT 18 /note= "phosphorylated"
FT 19 /note= "phosphorylated"
FT 35 /note= "phosphorylated"
FT W09517518-A1.
FT 29-JUN-1995.
FT 20-DEC-1994; FOI500.
FT 23-DEC-1993; FR-015764.
FT (INRG ) INST NAT RECH AGRONOMIQUE.
FT Briand L, Chobert J, Haertle T;
FT WPI; 95-240679/31.
FT New esterified amino acids, peptide(s) and their mixts. - prepd. by
FT esterification of protein then enzymatic hydrolysis, useful as
FT ingredients and additives in foods, pharmaceuticals and cosmetics
FT Claim 7; Fig 7 and 18; 47pp; French.
FT The native form of bovine beta-casein A1 contains various pepsin
FT cleavage sites. Esterification of the protein with methanol or ethanol
FT results in a form of beta-casein contg. additional, non-conventional
FT pepsin cleavage sites (See Features Table). Esterified peptides and
FT amino acids (and their mixtures) resulting from hydrolysis of an
FT esterified protein (pref. beta-lactoglobulin or beta-casein) are
FT claimed. The hydrolysis products are useful as ingredients,
FT additives or active agents in foods, pharmaceuticals and cosmetics.
FT Sequence 209 AA;
FT SQ 5 A; 4 R; 5 N; 4 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;
FT SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;
FT CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq
FT Initial Score = 12 Optimized Score = 12 Significance = 1.29
FT Residue Identity = 100% Matches = 12 Mismatches = 0

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OKIHFAQTQSLVYFPGPIHNSLPQNIPPLT  
50 X 60 70

ST-70C-0T Qd

XX 27-DEC-1996; 96WO-EP05846.  
 XX  
 XX 27-DEC-1995; 95IT-0RM0850.  
 XX  
 XX (BIOS-) BIOSYSTEMA DI SARAPANI & C SAS PIER LUIG.  
 XX (MIDI-) MIDIA LTD.  
 XX  
 XX Pozzilli P;  
 XX  
 XX WPI; 1997-363622/33.  
 XX  
 XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 XX food or pharmaceutical products for prevention of insulin dependent  
 XX diabetes, particularly in early infancy  
 XX  
 XX Claim 5; Page 4; 34pp; English.  
 XX  
 XX This sequence represents an immunogenic peptide from the A2 variant of  
 XX beta-casein found in both Bos taurus and Bos indicus. The peptide  
 XX contains a motif (see AAW31288) corresponding to amino acids 63-68 of  
 XX the A2 beta casein protein and is found to be capable of mimicking a  
 XX fragment of the GLUT2 protein found in insulin producing cells of the  
 XX pancreas. There is a known correlation between exposure to cow's milk and  
 XX the development of insulin-dependent diabetes which could possibly be  
 XX linked to this molecular mimicry. Dietary or pharmaceutical products  
 XX derived from milk substantially free of non-human beta casein or  
 XX containing modified beta-casein without this motif could be used in diets  
 XX for the prevention of insulin dependent diabetes particularly during  
 XX early infancy.  
 XX  
 XX SQ Sequence 12 AA;

AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063  
 Initial Score = 11 Optimized Score = 11 Significance = 1.03  
 Residue Identity = 91% Matches = 11 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X 10 X  
 SLVYPPGPPIH  
 |||||  
 SLVYPPGPPIH  
 X 10 X

8. US-09-095-639a-3 (1-12)

P02666 Beta casein precursor.

Orig of: p02666 check: 8112 from: 1 to: 224

ID CASB\_BOVIN STANDARD; PRT; 224 AA.  
 AC P02666;  
 DT 21-JUL-1986 (Rel. 01, Created)  
 DT 01-MAR-1989 (Rel. 10, Last sequence update)  
 DT 01-MAR-2002 (Rel. 41, Last annotation update)  
 DE Beta casein precursor.  
 GN CSN2.  
 OS Bos taurus (Bovine).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
 OC Bovidae; Bovinae; Bos.  
 OC NCBI\_TaxID=9913;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;  
 RT "Primary structure of bovine beta-casein cDNA."  
 RL Mol. Biol. (Mosk) 21:214-222(1987).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RA MEDLINE=8818989; PubMed=2833669;  
 RA Stewart A.F., Bonsing J., Beattie C.W., Shah F., Willis I.M.,  
 RA Mackinlay A.G.;

RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein  
 RL cDNAs: comparisons with related sequences in other species.";  
 RN Mol. Biol. Evol. 4:231-241(1987).  
 RP [3]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=90147279; PubMed=3271384;  
 RA Bonsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;  
 RT "Complete nucleotide sequence of the bovine beta-casein gene.";  
 RN Aust. J. Biol. Sci. 41:527-537(1988).  
 RP [4]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=87128158; PubMed=3814153;  
 RA Jimenez-Flores R., Kang Y.C., Richardson T.;  
 RT "Cloning and sequence analysis of bovine beta-casein cDNA.";  
 RN Biochem. Biophys. Res. Commun. 142:617-621(1987).  
 RP [5]  
 RP SEQUENCE FROM N.A. (VARIANT A3).  
 RC TISSUE=Mammary gland;  
 RX MEDLINE=94068382; PubMed=8248100;  
 RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,  
 RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;  
 RT "Overproduction of bovine beta-casein in Escherichia coli and  
 RL engineering of its main chymosin cleavage site.";  
 RN Protein Eng. 6:763-770(1993).  
 RP [6]  
 RP SEQUENCE OF 16-224 (VARIANT A2).  
 RX MEDLINE=88152252; PubMed=3278933;  
 RA Carles C., Huet J.-C., Ribadeau-Dumas B.;  
 RT "A new strategy for primary structure determination of proteins:  
 RL application to bovine beta-casein.";  
 RN FEBS Lett. 229:265-272(1988).  
 RP [7]  
 RP SEQUENCE OF 16-224 (VARIANT A2).  
 RX MEDLINE=72233212; PubMed=4557764;  
 RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;  
 RT "Primary structure of bovine beta casein. Complete sequence.";  
 RN Eur. J. Biochem. 25:505-514(1972).  
 RP [8]  
 RP VARIANTS A1; B AND C.  
 RX MEDLINE=72214259; PubMed=5064450;  
 RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RT "Characterization of genetic variants of alpha-S1 and beta bovine  
 RL caseins.";  
 RN Eur. J. Biochem. 26:328-337(1972).  
 RP [9]  
 RP SEQUENCE OF 118-124 (VARIANT A3).  
 RX MEDLINE=71252171; PubMed=4997616;  
 RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
 RT "Localization in the peptide chain of bovine beta casein of the  
 RL His-Gln substitution differentiating the A2 and A3 genetic  
 RN variants.";  
 RN C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
 RP [10]  
 RP SEQUENCE OF 48-63 (VARIANT E).  
 RX MEDLINE=75005247; PubMed=4411121;  
 RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
 RT "The beta E variant and the phosphorylation code of bovine caseins.";  
 RN FEBS Lett. 45:3-5(1974).  
 RP [11]  
 RP SEQUENCE OF 68-105 FROM N.A.  
 RX MEDLINE=85155504; PubMed=6397405;  
 RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
 RA Sulimova G.E., Judinkova E.S., Gorodetsky S.I.;  
 RT "Identification of bacterial clones encoding bovine caseins by direct  
 RL immunological screening of the cDNA library.";  
 RN Gene 32:381-388(1984).  
 RP [12]  
 RP SEQUENCE OF 68-95 FROM N.A.  
 RX MEDLINE=86014005; PubMed=3900695;  
 RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
 RA Sulimova G.E.;  
 RT "Identification of bacterial clones coding for bovine caseins by  
 RL direct immunologic screening of the cDNA library.";

RL Mol. Biol. (Mosk) 19:955-963(1985).  
[13]  
RP SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE-20154951; PubMed-10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
beta-casein variant detected in Korean cattle.";  
RL Anim. Genet. 31:49-51(2000).  
[14]  
RP SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RA Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
casein by peptide mapping and mass spectrometric analysis.";  
RL Int. Dairy J. 8:967-972(1998).  
[15]  
RP SEQUENCE OF 160-171 (VARIANT F).  
RA MEDLINE-96118672; PubMed-7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
reversed-phase high-performance liquid chromatography and mass  
spectrometric analysis.";  
RL J. Chromatogr. A 711:141-150(1995).  
[16]  
RP SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE-93182023; PubMed-6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RL DNA 1:375-386(1982).  
[17]  
RP CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE-9500478; PubMed-6148101;  
RA Yan S.B., Mold F.;  
RT "Neoglycoproteins: In vitro introduction of glycosyl units at  
glutamines in beta-casein using transglutaminase.";  
RL Biochemistry 23:3759-3765(1984).  
CC -1- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
PROPERTIES OF THE CASEIN MICELLES.  
CC -1- SUBCELLULAR LOCATION: Extracellular.  
CC -1- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -1- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190  
AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
THE A2 VARIANT.  
CC -1- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -1- DATABASE: NAME-Protein Spotlight;  
NOTE-Issue 16 of November 2001;  
WWW="http://www.expasy.org/spotlight/articles/spt1t016.html".  
-----  
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EMBL: M16645; AAA30480.1; -  
EMBL: M5132; AAA30430.1; -  
EMBL: K01087; AAA30481.1; -  
EMBL: X06359; CAA29658.1; -  
EMBL: M55158; AAA30431.1; -  
EMBL: S67277; AAB29137.1; -  
EMBL: AF104929; AAD09813.1; -  
EMBL: AF104928; AAD09813.1; JOINED.  
DR EMBL: M64756; AAB59254.1; -  
DR PIR: A03110; KBB0A2.  
DR PIR: A25846; A25846.  
DR PIR: B29087; B29087.  
DR PIR: S01860; S01860.  
DR PIR: S02429; S02429.  
DR CarBank: CCSD:9067; -  
DR InterPro: IPR001588; Casein.

DR Pfam; PF00363; caseins; 1.  
DR PROSITE; PS00306; CASEIN\_ALPHA\_BETA; 1.  
KW Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224 BETA CASEIN.  
FT MOD\_RES 30 30 PHOSPHORYLATION.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 70 70 O-LINKED (GALNAC. .) (PARTIAL).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. .).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVRGPFPIIV -> DPSLLL (IN REF. 1).  
SQ SEQUENCE 224 AA; 25107 MW; FOBBDD8148A238AE CRC64;  
  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
  
Initial Score = 11 Optimized Score = 11 Significance = 1.03  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0  
  
X 10 X  
SLVYPPPGPIHN  
|||||||  
DKTHPFAQTQSLVYPPPGPIHNSLPQNIPLT  
70 X 80 X 90  
  
9. US-09-095-639A-3 (1-12)  
p02662 Alpha-S1 casein precursor.  
  
TOIG of: p02662 check: 2471 from: 1 to: 214  
  
ID CASL\_BOVIN STANDARD; PRT; 214 AA.  
AC P02662; Q28048;  
DT 21-JUL-1986 (Rel. 01, Created)  
DT 01-NOV-1990 (Rel. 16, Last sequence update)  
DT 01-MAR-2002 (Rel. 41, Last annotation update)  
DE Alpha-S1 casein precursor.  
GN CSNLSI.  
OS Bos taurus (Bovine).  
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;  
OC Bovidae; Bovinae; Bos.  
OX NCBI\_TaxID=9913;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE-84221403; PubMed-6328443;  
RA Stewart A.F., Willis I.M., Mackinlay A.G.;  
RT "Nucleotide sequences of bovine alpha S1- and kappa-casein cDNAs.";  
RL Nucleic Acids Res. 12:3895-3907(1984).  
RN [2]  
RP SEQUENCE FROM N.A.  
RA Nagao M., Maki M., Sasaki R., Chiba R.;  
RT "Isolation and sequence analysis of bovine alpha-S1-casein cDNA  
clone.";  
RL Agric. Biol. Chem. 48:1663-1667(1984).

[3] SEQUENCE FROM N.A.  
 RP MEDLINE=87049835; PubMed=3022833;  
 RA Gorodetskii S.I., Zakhar'ev V.M., Kyarshulite D.R., Kapelinskaya T.V.,  
 RA Skryabin K.G.;  
 RT "cDNA of cattle alpha S1-casein: cloning and nucleotide sequence.";  
 RL Biokhimiia 51:1641-1648(1986).  
 [4]  
 RP SEQUENCE FROM N.A.  
 RP MEDLINE=92051301; PubMed=1659736;  
 RA Koczan D., Hobom G., Seyfert H.M.;  
 RA "Genomic organization of the bovine alpha-S1 casein gene.";  
 RL Nucleic Acids Res. 19:5591-5596(1991).  
 [5]  
 RP SEQUENCE OF 55-130 FROM N.A.  
 RP MEDLINE=83182023; PubMed=6897774;  
 RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
 RA "Construction and identification by partial nucleotide sequence  
 RT analysis of bovine casein and beta-lactoglobulin cDNA clones";  
 RL DNA 1:375-386(1982).  
 [6]  
 RP SEQUENCE OF 122-214 FROM N.A.  
 RP MEDLINE=85178933; PubMed=3838718;  
 RA Kyarshulite D.R., Zakhar'ev V.M., Gorodetskii S.I.;  
 RA "Nucleotide sequence of the 3'-nontranslated region of the mRNA of  
 RT alpha S1-casein in cows.";  
 RL Dokl. Akad. Nauk SSSR 280:1433-1437(1985).  
 [7]  
 RP SEQUENCE OF 164-214 FROM N.A.  
 RP MEDLINE=94154154; PubMed=1343827;  
 RA Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;  
 RA "Cloning, mapping, and sequencing of 3' and its flanking region of  
 RT bovine alpha-S1 casein gene";  
 RL Chin. J. Biotechnol. 8:235-245(1992).  
 [8]  
 RP SEQUENCE OF 16-214 (VARIANT B).  
 RP MEDLINE=72063417; PubMed=4331376;  
 RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
 RA "Primary structure of bovine alpha-S1 casein. Complete sequence.";  
 RL Eur. J. Biochem. 23:41-51(1971).  
 [9]  
 RP REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).  
 RP MEDLINE=74082545; PubMed=4797901;  
 RA Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
 RA "Primary structure of alpha casein and of bovine beta casein.  
 RT Correction.";  
 RL Eur. J. Biochem. 40:323-323(1973).  
 [10]  
 RP SEQUENCE (VARIANT D).  
 RP MEDLINE=72214259; PubMed=5064450;  
 RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RA "Characterization of genetic variants of alpha-S1 and beta bovine  
 RT caseins.";  
 RL Eur. J. Biochem. 26:328-337(1972).  
 [11]  
 RP SEQUENCE OF 23-49 (VARIANT A).  
 RP Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
 RA "Localization in the N-terminal part of bovine casein alpha-s1 of a  
 RT 13 amino-acid deletion that differentiates variant A from variants B  
 RT and C.";  
 RL FEBS Lett. 11:109-112(1970).  
 [12]  
 RP SEQUENCE OF 205-214 (VARIANT C).  
 RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
 RA "On the localization in the C-terminal sequence of bovine casein  
 RT alpha-s1 of a Glu/Gly substitution that differentiates the genetic  
 RT variants B and C.";  
 RL C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).  
 [13]  
 RP REVISION (VARIANT C).  
 RP Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
 RA C. R. Acad. Sci., D, Sci. Nat. 271:563-563(1970).  
 RL -!- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT

CC CALCIUM PHOSPHATE.  
 CC -!- SUBCELLULAR LOCATION: Extracellular.  
 CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
 CC -!- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.  
 CC -!- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.  
 CC -!- DATABASE: NAME-Worthington enzyme manual;  
 CC WWW="http://www.worthington-biochem.com/manual/C/CASA.html".  
 CC -!- DATABASE: NAME-Protein Spotlight;  
 CC NOTE-Issue 16 of November 2001;  
 CC WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
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 CC or send an email to license@isb-sib.ch).  
 CC -----  
 CC EMBL: X00564; CAB57792.1;  
 CC EMBL: M33123; AAA30428.1;  
 CC EMBL: M38641; AAA30429.1;  
 CC EMBL: X59856; CAA42516.1;  
 CC EMBL: K01084; AAA30478.1;  
 CC EMBL: M38658; AAA62707.1;  
 CC EMBL: S72388; AAD14099.1;  
 CC PIR: A03106; KABOSB.  
 CC PIR: A23071; A23071.  
 CC PIR: S22202; S22202.  
 CC PIR: S22575; S22575.  
 CC InterPro: IPR001588; Casein.  
 CC Pfam: PF00363; caseins: 1.  
 CC PROSITE: PS00306; CASEIN\_ALPHA\_BETA; 1.  
 CC Milk: Phosphorylation; Signal; Repeat.  
 CC SIGNAL 1 15  
 CC FT CHAIN 16 214 ALPHA-S1 CASEIN.  
 CC FT MOD\_RES 61 61 PHOSPHORYLATION.  
 CC FT MOD\_RES 63 63 PHOSPHORYLATION.  
 CC FT MOD\_RES 68 68 PHOSPHORYLATION (IN VARIANT D).  
 CC FT MOD\_RES 79 79 PHOSPHORYLATION.  
 CC FT MOD\_RES 81 81 PHOSPHORYLATION.  
 CC FT MOD\_RES 82 82 PHOSPHORYLATION.  
 CC FT MOD\_RES 83 83 PHOSPHORYLATION.  
 CC FT MOD\_RES 90 90 PHOSPHORYLATION.  
 CC FT MOD\_RES 130 130 PHOSPHORYLATION.  
 CC FT REPEAT 85 99  
 CC FT REPEAT 125 140  
 CC FT VARIANT 29 41 MISSING (IN VARIANT A).  
 CC FT VARIANT 68 68 A -> T (IN VARIANT D).  
 CC FT VARIANT 207 207 E -> G (IN VARIANT C).  
 CC FT CONFLICT 42 42 P -> L (IN REF. 3).  
 CC FT CONFLICT 50 50 E -> Q (IN REF. 4 AND 11).  
 CC FT CONFLICT 95 95 H -> Q (IN REF. 5).  
 CC FT CONFLICT 143 143 H -> D (IN REF. 3).  
 CC FT CONFLICT 203 203 S -> L (IN REF. 6).  
 CC FT CONFLICT 211 212 MP -> IS (IN REF. 3).  
 CC SQ SEQUENCE 214 AA; 24529 MW; F066B5C8AE55828B CRC64;  
 P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471  
 Initial Score = 6 Optimized Score = 7 Significance = -0.26  
 Residue Identity = 16% Matches = 2 Mismatches = 10  
 Gaps = 0 Conservative Substitutions = 0  
 X 10 X  
 SLVYPPFGPIHN  
 MKLLILTCLVAVALAKPKIKHQGLPQEV  
 10 20 30

10. US-09-095-639a-3 (1-12)  
 W31287 Bovine beta casein variant A1 immunogenic peptide

W31287 standard; peptide; 5 AA.  
W31287;  
05-MAR-1998 (first entry)  
Bovine beta casein variant A1 immunogenic peptide motif.  
Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
Bos taurus.  
WO9724371-AL.  
10-JUL-1997.  
27-DEC-1996; E05846.  
27-DEC-1995; IT-RM0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.  
Pozzilli P;  
WPI; 97-363622/33.  
Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
Claim 5; Page 3; 34pp; English.  
This sequence represents an immunogenic peptide motif from the A1 variant of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.  
Sequence 5 AA;  
AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114 ..  
Initial Score = 5 Optimized Score = 5 Significance = -0.52  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0  
X 10  
SLVYPPGPIHN  
|||||  
PGPIH  
X X  
12. US-09-095-639A-3 (1-12)  
W31293 Bovine beta casein immunogenic peptide motif 1.  
ID W31293 standard; peptide; 4 AA.  
AC W31293;  
DE 05-MAR-1998 (first entry)  
DT Bovine beta casein immunogenic peptide motif 1.  
KW Beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
Bos taurus.  
PN WO9724371-AL.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
PS Claim 10; Page 6; 34pp; English.  
This sequence represents an immunogenic peptide motif of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.  
Sequence 4 AA;  
SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
Initial Score = 4 Optimized Score = 4 Significance = -0.78

W31287 standard; peptide; 5 AA.  
W31287;  
05-MAR-1998 (first entry)  
Bovine beta casein variant A1 immunogenic peptide motif.  
Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
Bos taurus.  
WO9724371-AL.  
10-JUL-1997.  
27-DEC-1996; E05846.  
27-DEC-1995; IT-RM0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.  
Pozzilli P;  
WPI; 97-363622/33.  
Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy  
Claim 5; Page 3; 34pp; English.  
This sequence represents an immunogenic peptide motif from the A1 variant of beta-casein which is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.  
Sequence 5 AA;  
SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
Initial Score = 5 Optimized Score = 5 Significance = -0.52  
Residue Identity = 100% Matches = 5 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0  
X 10  
SLVYPPGPIHN  
|||||  
PGPIH  
X X  
11. US-09-095-639A-3 (1-12)  
aaw31287 Bovine beta casein variant A1 immunogenic peptide  
GIG of: aaw31287 check: 1114 from: 1 to: 5  
AAW31287 standard; peptide; 5 AA.  
AAW31287;  
05-MAR-1998 (first entry)  
Bovine beta casein variant A1 immunogenic peptide motif.  
Al variant beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.  
Bos taurus.  
WO9724371-AL.  
10-JUL-1997.  
27-DEC-1996; 96WO-EP05846.  
27-DEC-1995; 95IT-ORM0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.



Residue Identity = 100% Matches = 0  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYPPFGPIHN  
||||  
GPIH  
X X

13. US-09-095-639A-3 (1-12)  
aaw31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaw31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.

AC AAW31293;

05-MAR-1998 (first entry)

Bovine beta casein immunogenic peptide motif 1.

Beta casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

WO9724371-Al.

10-JUL-1997.

27-DEC-1996; 96WO-EP05846.

27-DEC-1995; 95IT-ORW0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
food or pharmaceutical products for prevention of insulin dependent  
diabetes, particularly in early infancy

Claim 10; Page 6; 34pp; English.

This sequence represents an immunogenic peptide motif of beta-casein  
which is capable of mimicking a fragment of the GLUT2 protein found in  
insulin producing cells of the pancreas. There is a known correlation  
between exposure to cow's milk and the development of insulin-dependent  
diabetes which could possibly be linked to this molecular mimicry.  
Dietary or pharmaceutical products derived from milk substantially free  
of non-human beta casein or containing modified beta-casein without this  
motif could be used in diets for the prevention of insulin dependent  
diabetes particularly during early infancy.

Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738

Initial Score = 4 Optimized Score = 4 Significance = -0.78  
Residue Identity = 100% Matches = 4 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYPPFGPIHN  
||||  
GPIH  
X X

14. US-09-095-639A-3 (1-12)  
W31288 Bovine beta casein variant A2 immunogenic peptide

W31288 standard; peptide; 5 AA.

05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide motif.  
A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

Bos indicus

WO9724371-Al.

10-JUL-1997.

27-DEC-1996; E05846.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

(MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 97-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
food or pharmaceutical products for prevention of insulin dependent  
diabetes, particularly in early infancy  
Claim 5; Page 4; 34pp; English.  
This sequence represents an immunogenic peptide motif from the A2 variant  
beta-casein found in both Bos taurus and Bos indicus (amino acid  
position 63-68). This motif is capable of mimicking a fragment of the  
GLUT2 protein found in insulin producing cells of the pancreas. There is  
a known correlation between exposure to cow's milk and the development of  
insulin-dependent diabetes which could possibly be linked to this  
molecular mimicry. Dietary or pharmaceutical products derived from milk  
substantially free of non-human beta casein or containing modified  
beta-casein without this motif could be used in diets for the prevention  
of insulin dependent diabetes particularly during early infancy.

Sequence 5 AA;

SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;  
SQ 1 I; 0 L; 0 K; 0 M; 0 F; 3 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = -0.78  
Residue Identity = 80% Matches = 4 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10  
SLVYPPFGPIHN  
||||  
PGPIP  
X X

15. US-09-095-639A-3 (1-12)  
aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5

AAW31288 standard; peptide; 5 AA.

AAW31288;

05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide motif.

A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.

Bos indicus

WO9724371-Al.

10-JUL-1997.

Mon Mar 3 11:50:09 2003

Initial Score = 4 Optimized Score = 4 Significance = -0.78  
 Residue Identity = 28% Matches = 2 Mismatches = 4  
 Gaps = 0 Conservative Substitutions = 1

XX 27-DEC-1996; 96WO-EP05846.  
 XX 27-DEC-1995; 95IT-OR0850.  
 XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 XX (MIDI-) MIDIA LTD.

XX Pozzilli P;  
 XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 XX Claim 5; Page 4; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A2 variant  
 CC beta-casein found in both Bos taurus and Bos indicus (amino acid  
 CC position 63-68). This motif is capable of mimicking a fragment of the  
 CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
 CC a known correlation between exposure to cow's milk and the development of  
 CC insulin-dependent diabetes which could possibly be linked to this  
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.

XX Sequence 5 AA;  
 SQ AAW31298 Length: 5 March 3, 2003 11:28 Type: P Check: 1154 ..

Initial Score = 4 Optimized Score = 4 Significance = -0.78  
 Residue Identity = 80% Matches = 4 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

XX 10  
 SLVYPPFGPIHN  
 IIII  
 PGPIP  
 X X

16. US-09-095-639A-3 (1-12)  
 R37103 Bovine milk beta-casein enzymatic fragment.

ID R37103 standard; peptide; 7 AA.  
 AC 21-MAY-1995 (first entry)

XX Bovine milk beta-casein enzymatic fragment.  
 XX Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
 XX wrinkles.

OS Bos Taurus.  
 PN J06166615-A.  
 PD 14-JUN-1994.

PF 01-DEC-1992; 321624.  
 PR 01-DEC-1992; JP-321624.

PA (POK) POLA CHEM IND INC.  
 DR WPI; 94-230615/28.

PT Cosmetics for treating skin disorders and wrinkles - containing  
 PT enzymatic hydrolysate of human or bovine milk beta-casein

PS Claim 2; Page 2; 7pp; Japanese  
 CC The invention relates to cosmetics containing human or bovine milk  
 CC beta-casein enzymatic hydrolysate. The cosmetics are used for  
 CC improving skin disorders and/or wrinkles. They are more effective  
 CC than previously used polysaccharides, sugar alcohols, glycerol,  
 CC glycols, etc

CC The present sequence is one component of the bovine milk beta-casein  
 CC enzymatic hydrolysate.

SQ Sequence 7 AA;  
 SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;

SQ 0 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
 CC Retrieved by bobyen on Thu 27 Feb 103 16:22:04-PST using FindSeq

17. US-09-095-639A-3 (1-12)  
 W31294 Bovine beta casein immunogenic peptide motif 2.

ID W31294 standard; peptide; 4 AA.  
 AC W31294; 1998 (first entry)

DE Bovine beta casein immunogenic peptide motif 2.  
 DE Beta-casein; immunogenic; molecular mimicry; cow;  
 KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.  
 PN W09724371-A1.

PD 10-JUL-1997; E05846.  
 PF 27-DEC-1995; IT-RM0850.

PR (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.

PI Pozzilli P;  
 DR WPI; 97-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy

PS Claim 10; Page 6; 34pp; English.  
 CC This sequence represents an immunogenic peptide motif found in bovine  
 CC beta casein. This motif is capable of mimicking a fragment of the  
 CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
 CC a known correlation between exposure to cow's milk and the development of  
 CC insulin-dependent diabetes which could possibly be linked to this  
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 4 AA;  
 SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;

SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobyen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 3 Optimized Score = 3 Significance = -1.03  
 Residue Identity = 75% Matches = 3 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

XX 10  
 SLVYPPFGPIHN  
 IIII  
 GPPI  
 X X

18. US-09-095-639A-3 (1-12)  
 aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

ID AAW31294 standard; peptide; 4 AA.  
 XX AAW31294;

AC AAW31294;  
 XX 05-MAR-1998 (first entry)

XX Bovine beta casein immunogenic peptide motif 2.  
 XX Beta-casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX OS Bos taurus.

XX PN W09724371-A1.

XX PD 10-JUL-1997.

XX PF 27-DEC-1996; 96WO-EP05846.

XX PR 27-DEC-1995; 95IT-ORM0850.

XX PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX PA (MIDI-) MIDIA LTD.

XX PI Pozzilli P;

XX DR WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mimicry with GLUT2 - used in food or pharmaceutical products for prevention of insulin dependent diabetes, particularly in early infancy

XX Claim 10; Page 6; 34pp; English.

CC This sequence represents an immunogenic peptide motif found in bovine beta casein. This motif is capable of mimicking a fragment of the GLUT2 protein found in insulin producing cells of the pancreas. There is a known correlation between exposure to cow's milk and the development of insulin-dependent diabetes which could possibly be linked to this molecular mimicry. Dietary or pharmaceutical products derived from milk substantially free of non-human beta casein or containing modified beta-casein without this motif could be used in diets for the prevention of insulin dependent diabetes particularly during early infancy.

XX SQ Sequence 4 AA;

. AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..  
Initial Score = 3 Optimized Score = -1.03  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYPPGPIHN  
|||  
GPIP  
X X





SO 1 I; 1 L; 0 K; 0 M; 1 F; 4 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 12 Optimized Score = 12 Significance = 1.33  
 Residue Identity = 100% Matches = 12 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X 10 X  
 SLVYPPPGPIP  
 |||||  
 SLVYPPPGPIP  
 X 10 X

2. US-09-095-639A-4 (1-12)  
 aaw31290 Bovine beta casein variant A2 immunogenic peptide.

TOIG of: aaw31290 check: 6063 from: 1 to: 12

AAW31290 standard; peptide; 12 AA.

AAW31290;

05-MAR-1998 (first entry)

Bovine beta casein variant A2 immunogenic peptide.

A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
 milk product; insulin-dependent diabetes; GLUT2; diet.

Bos taurus.  
 Bos indicus.

W09724371-A1.

10-JUL-1997.

27-DEC-1996; 96WO-EP05846.

27-DEC-1995; 95IT-ORM0850.

(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 (MIDI-) MIDIA LTD.

Pozzilli P;

WPI; 1997-363622/33.

Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 food or pharmaceutical products for prevention of insulin dependent  
 diabetes, particularly in early infancy

Claim 5; Page 4; 34pp; English.

This sequence represents an immunogenic peptide from the A2 variant of  
 beta-casein found in both Bos taurus and Bos indicus. The peptide  
 contains a motif (see AAW31288) corresponding to amino acids 63-68 of  
 the A2 beta casein protein and is found to be capable of mimicking a  
 fragment of the GLUT2 protein found in insulin producing cells of the  
 pancreas. There is a known correlation between exposure to cow's milk and  
 the development of insulin-dependent diabetes which could possibly be  
 linked to this molecular mimicry. Dietary or pharmaceutical products  
 derived from milk substantially free of non-human beta casein or  
 containing modified beta-casein without this motif could be used in diets  
 for the prevention of insulin dependent diabetes particularly during  
 early infancy.

Sequence 12 AA;

AAW31290 Length: 12 March 3, 2003 11:29 Type: P Check: 6063

Initial Score = 12 Optimized Score = 12 Significance = 1.33  
 Residue Identity = 100% Matches = 12 Mismatches = 0

Gaps

X 10 X  
 SLVYPPPGPIP  
 |||||  
 SLVYPPPGPIP  
 X 10 X

3. US-09-095-639A-4 (1-12)  
 p02666 Beta casein precursor.

TOIG of: p02666 check: 8112 from: 1 to: 224

ID CASB\_BOVIN STANDARD; PRT; 224 AA.  
 AC P02666;

DT 21-JUL-1986 (Rel. 01, Created)

DT 01-MAR-1989 (Rel. 10, Last sequence update)

DT 01-MAR-2002 (Rel. 41, Last annotation update)

DE Beta casein precursor.

GN CSN2.

OS Bos taurus (Bovine).

OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidae;

OC Bovidae; Bovinae; Bos.

OX NCBI\_TaxID=9913;

RN [1]

RP SEQUENCE FROM N.A.

RA Baev A.A., Smirnov I.K., Gorodetsky S.I.;

RT "Primary structure of bovine beta-casein cDNA.";

RL Mol. Biol. (Mosk) 21:214-222(1987).

RN [2]

RP SEQUENCE FROM N.A.

RX MEDLINE=88188989; PubMed=2833669;

RA Stewart A.F., Bomsing J., Beattie C.W., Shah F., Willis I.M.,

RA Mackinlay A.G.;

RT "Complete nucleotide sequences of bovine alpha S2- and beta-casein

cDNAs: comparisons with related sequences in other species.";

RL Mol. Biol. Evol. 4:231-241(1987).

RN [3]

RP SEQUENCE FROM N.A.

RX MEDLINE=90147279; PubMed=3271384;

RA Bomsing J., Ring J.M., Stewart A.F., Mackinlay A.G.;

RT "Complete nucleotide sequence of the bovine beta-casein gene.";

RL Aust. J. Biol. Sci. 41:527-537(1988).

RN [4]

RP SEQUENCE FROM N.A.

RX MEDLINE=87128158; PubMed=3814153;

RA Jimenez-Flores R., Kang Y.C., Richardson T.;

RT "Cloning and sequence analysis of bovine beta-casein cDNA.";

RL Biochem. Biophys. Res. Commun. 142:617-621(1987).

RN [5]

RP SEQUENCE FROM N.A. (VARIANT A3).

RC TISSUE=Mammary gland;

RX MEDLINE=94068382; PubMed=8248100;

RA Simons G., van den Heuvel W., Reynen T., Frijters A., Rutten G.,

RA Slangen C.J., Groenen M., de Vos W.M., Siezen R.J.;

RT "Overproduction of bovine beta-casein in Escherichia coli and

engineering of its main chymosin cleavage site.";

RL Protein Eng. 6:763-770(1993).

RN [6]

RP SEQUENCE OF 16-224 (VARIANT A2).

RX MEDLINE=88152252; PubMed=3278933;

RA Carles C., Huet J.-C., Ribadeau-Dumas B.;

RT "A new strategy for primary structure determination of proteins:

application to bovine beta-casein.";

RL FEBS Lett. 229:265-272(1988).

RN [7]

RP SEQUENCE OF 16-224 (VARIANT A2).

RX MEDLINE=7223212; PubMed=4557764;

RA Ribadeau-Dumas B., Brignon G., Grosclaude F., Mercier J.-C.;

RT "Primary structure of bovine beta casein. Complete sequence.";

RL Eur. J. Biochem. 25:505-514(1972).

[8] VARIANTS A1; B AND C.  
RX MEDLINE=72214259; PubMed=5064450;  
RA Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
RT "Characterization of genetic variants of alpha-S1 and beta bovine  
RT caseins.";  
RL Eur. J. Biochem. 26:328-337(1972).  
[9]  
RN SEQUENCE OF 118-124 (VARIANT A3).  
RX MEDLINE=71252171; PubMed=4997616;  
RA Ribadeau-Dumas B., Grosclaude F., Mercier J.-C.;  
RT "Localization in the peptide chain of bovine beta casein of the  
RT His-Gln substitution differentiating the A2 and A3 genetic  
RT variants.";  
RL C. R. Acad. Sci., D, Sci. Nat. 270:2369-2372(1970).  
[10]  
RN SEQUENCE OF 48-63 (VARIANT E).  
RX MEDLINE=75005247; PubMed=4411121;  
RA Grosclaude F., Mahe M.-F., Voglino G.-F.;  
RT "The beta E variant and the phosphorylation code of bovine caseins.";  
RL FEBS Lett. 45:3-5(1974).  
[11]  
RN SEQUENCE OF 68-105 FROM N.A.  
RX MEDLINE=85155504; PubMed=6397405;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Sulimova G.E., Judinkova E.S., Gorodetsky S.I.;  
RT "Identification of bacterial clones encoding bovine caseins by direct  
RT immunological screening of the cDNA library.";  
RL Gene 32:381-388(1984).  
[12]  
RN SEQUENCE OF 68-95 FROM N.A.  
RX MEDLINE=86014005; PubMed=3900695;  
RA Ivanov V.N., Kershulite D.R., Bayev A.A., Akhundova A.A.,  
RA Sulimova G.E.;  
RT "Identification of bacterial clones coding for bovine caseins by  
RT direct immunologic screening of the cDNA library.";  
RL Mol. Biol. (Mosk) 19:955-963(1985).  
[13]  
RN SEQUENCE OF 18-57 FROM N.A., AND SEQUENCE OF 16-224 (VARIANT H).  
RX MEDLINE=20154951; PubMed=10690361;  
RA Han S.K., Shin Y.C., Byun H.D.;  
RT "Biochemical, molecular and physiological characterization of a new  
RT beta-casein variant detected in Korean cattle.";  
RL Anim. Genet. 31:49-51(2000).  
[14]  
RN SEQUENCE OF 125-195 (VARIANTS A1 AND G).  
RA Dong C., Ng-Kwai-Hang K.F.;  
RT "Characterization of a non-electrophoretic genetic variant of beta-  
RT casein by peptide mapping and mass spectrometric analysis.";  
RL Int. Dairy J. 8:967-972(1998).  
[15]  
RN SEQUENCE OF 160-171 (VARIANT F).  
RX MEDLINE=96118672; PubMed=7496485;  
RA Visser S., Slangen C.J., Lagerwerf F.M., Van Dongen W.D.,  
RA Haverkamp J.;  
RT "Identification of a new genetic variant of bovine beta-casein using  
RT reversed-phase high-performance liquid chromatography and mass  
RT spectrometric analysis.";  
RL J. Chromatogr. A 711:141-150(1995).  
[16]  
RN SEQUENCE OF 170-184 FROM N.A.  
RX MEDLINE=83182023; PubMed=6897774;  
RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
RT "Construction and identification by partial nucleotide sequence  
RT analysis of bovine casein and beta-lactoglobulin cDNA clones.";  
RL DNA 1:375-386(1982).  
[17]  
RN CARBOHYDRATE-LINKAGE SITES.  
RX MEDLINE=85000478; PubMed=6148101;  
RA Yan S.B., Wolf F.;  
RT "Neoglycoproteins: in vitro introduction of glycosyl units at  
RT glucamines in beta-casein using transglutaminase.";  
RL Biochemistry 23:3759-3765(1984).

CC -!- FUNCTION: IMPORTANT ROLE IN DETERMINATION OF THE SURFACE  
CC PROPERTIES OF THE CASEIN MICELLES.  
CC -!- SUBCELLULAR LOCATION: Extracellular.  
CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
CC -!- POLYMORPHISM: LEU-152 IS PRESENT IN THE VARIANTS F AND G; GLN-190  
CC AND GLU-210 ARE PRESENT IN THE VARIANT H. THE SEQUENCE SHOWN IS  
CC THE A2 VARIANT.  
CC -!- SIMILARITY: BELONGS TO THE BETA-CASEIN FAMILY.  
CC -!- DATABASE: NAME-Protein Spotlight;  
CC NOTE-Issue 16 of November 2001;  
CC WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".  
CC  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
CC between the Swiss Institute of Bioinformatics and the EMBL Outstation -  
CC the European Bioinformatics Institute. There are no restrictions on its  
CC use by non-profit institutions as long as its content is in no way  
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CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC  
CC EMBL; M16645; AAA30480.1; -  
CC EMBL; M15132; AAA30430.1; -  
CC EMBL; K01087; AAA30481.1; -  
CC EMBL; X06359; CAA29658.1; -  
CC EMBL; M55158; AAA30431.1; -  
CC EMBL; S67277; AAB29137.1; -  
CC EMBL; AF104929; AAD09813.1; -  
CC EMBL; AF104928; AAD09813.1; JOINED.  
CC EMBL; M64756; AAB59254.1; -  
CC PIR; A03110; KBOA2.  
CC PIR; A25846; A25846.  
CC PIR; B29087; B29087.  
CC PIR; S01860; S01860.  
CC PIR; S02429; S02429.  
CC CarBank; CCSD:9067; -  
CC InterPro; IPR001588; Casein.  
CC Pfam; PF00363; caseins; 1.  
CC PROSITE; P500306; CASEIN\_ALPHA\_BETA; 1.  
CC Milk; Phosphorylation; Glycoprotein; Signal; Polymorphism.  
FT SIGNAL 1 15  
FT CHAIN 16 224 BETA CASEIN.  
FT MOD\_RES 30 30 PHOSPHORYLATION.  
FT MOD\_RES 32 32 PHOSPHORYLATION.  
FT MOD\_RES 33 33 PHOSPHORYLATION.  
FT MOD\_RES 34 34 PHOSPHORYLATION.  
FT MOD\_RES 50 50 PHOSPHORYLATION (EXCEPT IN VARIANT C).  
FT CARBOHYD 70 70 O-LINKED (GALNAC. . .) (PARTIAL).  
FT CARBOHYD 72 72 O-LINKED (GALNAC. . .).  
FT CARBOHYD 95 95 O-LINKED (GALNAC. . .).  
FT CARBOHYD 183 183 O-LINKED (GALNAC. . .).  
FT VARIANT 40 40 R -> C (IN VARIANT H).  
FT VARIANT 51 51 E -> K (IN VARIANT E).  
FT VARIANT 52 52 E -> K (IN VARIANT C).  
FT VARIANT 82 82 P -> H (IN VARIANTS A1, B, C, F AND G).  
FT VARIANT 103 103 L -> I (IN VARIANT H).  
FT VARIANT 121 121 H -> Q (IN VARIANT A3).  
FT VARIANT 132 132 E -> Q (IN VARIANTS A1 AND G).  
FT VARIANT 137 137 S -> R (IN VARIANT B).  
FT VARIANT 152 153 LP -> PL (IN VARIANTS A1 AND H).  
FT VARIANT 153 153 P -> L (IN VARIANT G).  
FT VARIANT 167 167 P -> L (IN VARIANT F).  
FT VARIANT 190 190 Q -> E (IN VARIANTS A1 AND G).  
FT CONFLICT 108 108 M -> L (IN REF. 4 AND 7).  
FT CONFLICT 210 210 E -> Q (IN REF. 4 AND 7).  
FT CONFLICT 215 224 PVKGPFPPIIV -> DPSLLI (IN REF. 1).  
SQ SEQUENCE 224 AA; 25107 MW; F0BBD8148A238AE CRC64;  
P02666 Length: 224 February 28, 2003 14:33 Type: P Check: 8112 ..  
Initial Score = 12 Optimized Score = 12 Significance = 1.33  
Residue Identity = 100% Matches = 12 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
DKIHFAQTOSLVYPPFGPIPNSLFQNIPLT  
70 X 80 X 90

#### 4. US-09-095-639A-4 (1-12) W31289 Bovine beta casein variant A1 immunogenic peptide.

ID W31289 standard; peptide; 12 AA.  
AC W31289;  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A1 immunogenic peptide.  
KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
PN Bos taurus.  
PD WO9724371-A1.  
27-DEC-1996; E05846.  
27-DEC-1995; IT-RM0850.  
(BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilll P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PS Claim 5; Page 3; 34pp; English.  
CC This sequence represents an immunogenic peptide from the A1 variant of  
CC beta-casein which contains a motif (see W31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk and  
CC the development of insulin-dependent diabetes which could possibly be  
CC linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in diets  
CC for the prevention of insulin dependent diabetes particularly during  
CC early infancy.  
SQ Sequence 12 AA:  
SQ 0 A; 0 R; 1 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
SQ 1 I; 1 L; 0 K; 0 M; 1 F; 3 P; 1 S; 0 T; 0 W; 1 Y; 1 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 11 Optimized Score = 11 Significance = 1.06  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
SLVYPPFGPIPN  
X 10 X

#### 5. US-09-095-639A-4 (1-12) aaw31289 Bovine beta casein variant A1 immunogenic peptide.

TOIG of: aaw31289 check: 5975 from: 1 to: 12

ID AAW31289 standard; peptide; 12 AA.  
AC AAW31289;  
XX  
XX  
DT 05-MAR-1998 (first entry)  
DE Bovine beta casein variant A1 immunogenic peptide.  
XX

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;  
KW milk product; Insulln-dependent diabetes; GLUT2; diet.  
XX  
OS Bos taurus.  
XX

PN WO9724371-A1.  
XX  
PD 10-JUL-1997.  
XX  
PF 27-DEC-1996; 96WO-EP05846.  
XX  
PR 27-DEC-1995; 95IT-OR0850.  
XX  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
XX  
PI Pozzilll P;  
XX  
DR WPI; 1997-363622/33.  
XX  
PT beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
XX  
PS Claim 5; Page 3; 34pp; English.  
XX

CC This sequence represents an immunogenic peptide from the A1 variant of  
CC beta-casein which contains a motif (see AAW31287) capable of mimicking a  
CC fragment of the GLUT2 protein found in insulin producing cells of the  
CC pancreas. There is a known correlation between exposure to cow's milk  
CC and the development of insulin-dependent diabetes which could possibly  
CC be linked to this molecular mimicry. Dietary or pharmaceutical products  
CC derived from milk substantially free of non-human beta casein or  
CC containing modified beta-casein without this motif could be used in  
CC diets for the prevention of insulin dependent diabetes particularly  
CC during early infancy.  
XX  
SQ Sequence 12 AA;

AAW31289 Length: 12 March 3, 2003 11:28 Type: P Check: 5975 ..  
Initial Score = 11 Optimized Score = 11 Significance = 1.06  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

X 10 X  
SLVYPPFGPIPN  
|||||  
SLVYPPFGPIPN  
X 10 X

#### 6. US-09-095-639A-4 (1-12) R95609 Bovine beta casein A1 variant.

ID R95609 standard; protein; 209 AA.  
AC R95609;  
DT 26-NOV-1996 (first entry)  
DE Bovine beta casein A1 variant.  
KW Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
KW butter; cheese; cream.  
OS Bos taurus.  
FH Key Location/Qualifiers  
FT region 63..68  
FT /label= Diabetogenic hexapeptide.

PD WO9614577-A1.  
PD 17-MAY-1996.  
PF 03-NOV-1995; NZ0114.  
PR 04-NOV-1994; NZ-264862.  
PA (NACH-) NAT CHILD HEALTH RES FOUND.  
PA (NZDA-) NEW ZEALAND DAIRY BOARD.  
PI Elliott RB, Hill JP;  
DR WPI: 96-251885/25

PT Selecting non-diabetogenic milk and milk prods. - by testing milk or  
PT cows for the presence of non-diabetogenic variants of beta-casein  
PS Disclosure; Figure 2; 28pp; English.  
CC A method for selecting milk for feeding to diabetes susceptible  
CC individuals comprises testing milk from identified cows for the



CC presence of variants of beta casein and selecting those cows whose  
CC milk contains non-diabetogenic variants and milking these cows  
CC separately. The milk and milk products obtained can reduce the risk  
CC of susceptible individuals contracting Type-1 diabetes.  
SQ Sequence 209 AA;  
SQ 5 A; 4 R; 4 N; 5 D; 0 C; 21 Q; 18 E; 0 Z; 5 G; 6 H;  
SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;  
CC Retrieved by bobrryn on Thu 27 Feb 103 16:22:05-PST using FindSeq  
Initial Score = 11 Optimized Score = 11 Significance = 1.06  
Residue Identity = 91% Matches = 11 Mismatches = 1  
Caps = 0 Conservative Substitutions = 0  
X 10 X  
SLVYPPFGPIPN  
|||||||  
DKIHFAQTSLVYPPFGPIHNSLPQNIPLT  
50 X 60 70  
US-09-095-639A-4 (1-12)  
R80281 Methyl or ethyl esterified bovine beta-casein A1.  
ID R80281 standard; protein; 209 AA.  
AC R80281;  
DT 14-FEB-1996 (first entry)  
DE Methyl or ethyl esterified bovine beta-casein A1.  
KW Bovine; beta-casein; ethyl esterification; pepsin hydrolysis;  
KW proteolysis; peptide ester; food; pharmaceutical; cosmetics.  
OS Bos taurus.  
FH Key  
FT Location/Qualifiers  
FT 1..209  
FT /note= "5% esterified by methanol or by  
FT ethanol, resulting in atypical pepsin  
FT cleavage sites, in addition to the  
FT naturally occurring (native) sites"  
FT 4..5  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 5..6  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl ester of beta-casein"  
FT 11..12  
FT cleavage\_site  
FT /note= "newly identified pepsin cleavage site in  
FT methyl ester of beta-casein"  
FT 15..16  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 44..45  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 45..46  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 55..56  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 57..58  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 58..59  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 72..73  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 73..74  
FT cleavage\_site  
FT /note= "newly identified pepsin cleavage site in  
FT methyl ester of beta-casein"  
FT 80..81  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 93..94  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT 125..126  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"

FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 126..127  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 127..128  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 141..142  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein"  
FT 142..143  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT 156..157  
FT cleavage\_site  
FT /note= "newly identified pepsin cleavage site in  
FT ethyl ester of beta-casein"  
FT 162..163  
FT cleavage\_site  
FT /note= "newly identified pepsin cleavage site in  
FT ethyl ester of beta-casein"  
FT 163..164  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT 164..165  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 188..189  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl ester of beta-casein"  
FT 189..190  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT 190..191  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in ethyl ester of beta-casein"  
FT 191..192  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT 192..193  
FT cleavage\_site  
FT /note= "pepsin cleavage site in native protein and  
FT in methyl and ethyl esters of beta-casein"  
FT 198..199  
FT cleavage\_site  
FT /note= "newly identified pepsin cleavage site in  
FT methyl and ethyl esters of beta-casein"  
FT 207..208  
FT cleavage\_site  
FT /note= "newly identified pepsin cleavage site in  
FT methyl ester of beta-casein"  
FT 2..25  
FT peptide  
FT /label= A  
FT /note= "tryptic peptide from native protein"  
FT 26..28  
FT peptide  
FT /label= B  
FT /note= "tryptic peptide from native protein"  
FT 29..32  
FT peptide  
FT /label= C  
FT /note= "tryptic peptide from native protein"  
FT 33..48  
FT peptide  
FT /label= D  
FT /note= "tryptic peptide from native protein"  
FT 49..97  
FT peptide  
FT /label= E  
FT /note= "tryptic peptide from native protein"  
FT 100..105  
FT peptide  
FT /label= F  
FT /note= "tryptic peptide from native protein"  
FT 106..107  
FT peptide  
FT /label= G  
FT /note= "tryptic peptide from native protein"  
FT 108..113  
FT peptide  
FT /label= H  
FT /note= "tryptic peptide from native protein"  
FT 114..169  
FT peptide  
FT /label= I  
FT /note= "tryptic peptide from native protein"  
FT 170..176  
FT peptide  
FT /label= J  
FT /note= "tryptic peptide from native protein"  
FT 177..183  
FT peptide

FT /label= K  
 FT /note= "tryptic peptide from native protein"  
 FT 184..202  
 FT /label= L  
 FT /note= "tryptic peptide from native protein"  
 FT 203..209  
 FT /label= N  
 FT /note= "tryptic peptide from native protein"  
 FT 15  
 FT /note= "phosphorylated"  
 FT 17  
 FT /note= "phosphorylated"  
 FT 18  
 FT /note= "phosphorylated"  
 FT 19  
 FT /note= "phosphorylated"  
 FT 35  
 FT /note= "phosphorylated"  
 FT  
 FT WO9517518-A1.  
 FT 29-JUN-1995.  
 FT 20-DEC-1994; F01500.  
 FT 23-DEC-1993; FR-015764.  
 FT (INRG ) INST NAT RECH AGRONOMIQUE.  
 FT Briand L, Chobert J, Haertle T;  
 FT WPI; 95-240679/31.  
 FT New esterified amino acids, peptide(s) and their mixts. - prepd. by  
 FT esterification of protein, then enzymatic hydrolysis, useful as  
 FT ingredients and additives in foods, pharmaceuticals and cosmetics  
 FT Claim 7; Fig 7 and 18; 47pp; French.  
 FT The native form of bovine beta-casein A1 contains various pepsin  
 FT cleavage sites. Esterification of the protein with methanol or ethanol  
 FT results in a form of beta-casein contg. additional, non-conventional  
 FT pepsin cleavage sites (see Features Table). Esterified peptides and  
 FT amino acids (and their mixtures) resulting from hydrolysis of an  
 FT esterified protein (pref. beta-lactoglobulin or beta-casein) are  
 FT claimed. The hydrolysis products are useful as ingredients.  
 FT additives or active agents in foods, pharmaceuticals and cosmetics.  
 FT SQ Sequence 209 AA;  
 SQ 5 A; 4 R; 5 D; 0 B; 0 C; 20 Q; 19 E; 0 Z; 5 G; 6 H;  
 SQ 10 I; 22 L; 11 K; 6 M; 9 F; 34 P; 16 S; 9 T; 1 W; 4 Y; 19 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq

Initial Score = 11 Optimized Score = 11 Significance = 1.06  
 Residue Identity = 91% Matches = 11 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X 10 X  
 SLVYPPFGPIPN  
 |||||  
 DKIHFFAQTSLVYPPFGPIHNSLPQNIPPLT  
 50 X 60 70

8. US-09-095-639A-4 (1-12)  
 aar95609 Bovine beta casein A1 variant.

TOIG of: aar95609 check: 2014 from: 1 to: 209

AAR95609 standard; protein; 209 AA.

AAR95609;

26-NOV-1996 (first entry)

Bovine beta casein A1 variant.

Milk; beta casein; diabetogenic; diabetes; cow; milk products;  
 butter; Cheese; cream.

Bos taurus.

Key Location/Qualifiers  
 Region 63..68

FT /label= Diabetogenic hexapeptide.  
 XX WO9614577-A1.  
 XX 17-MAY-1996.  
 XX  
 XX 03-NOV-1995; 95WO-NZ00114.  
 XX 04-NOV-1994; 94NZ-0264862.  
 XX (NACH-) NAT CHILD HEALTH RES FOUND.  
 XX (NZDA-) NEW ZEALAND DAIRY BOARD.  
 XX Elliott RB, Hill JP;  
 XX WPI; 1996-251885/25.  
 XX

Selecting non-diabetogenic milk and milk prods. - by testing milk or  
 cows for the presence of non-diabetogenic variants of beta-casein

Disclosure; Figure 2; 28pp; English.

A method for selecting milk for feeding to diabetes susceptible  
 individuals comprises testing milk from identified cows for the  
 presence of variants of beta casein and selecting those cows whose  
 milk contains non-diabetogenic variants and milking these cows  
 separately. The milk and milk products obtained can reduce the risk  
 of susceptible individuals contracting Type-1 diabetes.

SQ Sequence 209 AA;

AAR95609 Length: 209 March 3, 2003 11:28 Type: P Check: 2014 ..

Initial Score = 11 Optimized Score = 11 Significance = 1.06  
 Residue Identity = 91% Matches = 11 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X 10 X  
 SLVYPPFGPIPN  
 |||||  
 DKIHFFAQTSLVYPPFGPIHNSLPQNIPPLT  
 50 X 60 70

9. US-09-095-639A-4 (1-12)

W31288 Bovine beta casein variant A2 immunogenic peptide

W31288 standard; peptide; 5 AA.

ID W31288;  
 AC 05-MAR-1998 (first entry)  
 DE Bovine beta casein variant A2 immunogenic peptide motif.  
 KW A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
 OS milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

OS Bos indicus

PN WO9724371-A1.

PF 27-DEC-1996; E05846.

PR 27-DEC-1995; IT-RM0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

PA (MIDI-) MIDIA LTD.

PI Pozzilli P;

DR WPI; 97-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 food or pharmaceutical products for prevention of insulin dependent

PT diabetes, particularly in early infancy

PS Claim 5; Page 4; 34pp; English.

CC This sequence represents an immunogenic peptide motif from the A2 variant  
 beta-casein found in both Bos taurus and Bos indicus (amino acid  
 position 63-68). This motif is capable of mimicking a fragment of the  
 GLUT2 protein found in insulin producing cells of the pancreas. There is  
 a known correlation between exposure to cow's milk and the development of  
 insulin-dependent diabetes which could possibly be linked to this

CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.  
 SQ Sequence 5 AA:  
 SQ 0 A; 0 R; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 G; 0 I; 0 L; 0 M; 0 N; 0 P; 0 S; 0 T; 0 V; 0 W; 0 Y; 0 Z;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 3 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 5 Optimized Score = 5 Significance = -0.53  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X 10  
 SLVYPPFGPIP  
 |||||  
 PGP  
 X X

US-09-095-639A-4 (1-12)  
 aaw31288 Bovine beta casein variant A2 immunogenic peptide

TOIG of: aaw31288 check: 1154 from: 1 to: 5  
 ID AAW31288 standard; peptide; 5 AA.

AC AAW31288;  
 XX  
 XX 05-MAR-1998 (first entry)  
 XX Bovine beta casein variant A2 immunogenic peptide motif.  
 XX A2 variant beta-casein; immunogenic; molecular mimicry; cow;  
 XX milk product; insulin-dependent diabetes; GLUT2; diet.  
 XX Bos taurus.  
 XX Bos indicus  
 XX WO9724371-AL.  
 XX 10-JUL-1997.  
 XX 27-DEC-1996; 96WO-EP05846.  
 XX 27-DEC-1995; 95IT-OR0850.  
 XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PTER LUIG.  
 XX (MIDI-) MIDIA LTD.  
 XX Pozzilli P;  
 XX WPI; 1997-363622/33.

XX Beta-casein or fragments not showing mlmrcy with GLUT2 - used in  
 XX food or pharmaceutical products for prevention of insulin dependent  
 XX diabetes, particularly in early infancy  
 XX Claim 5; Page 4; 34pp; English.

XX This sequence represents an immunogenic peptide motif from the A2 variant  
 XX beta-casein found in both Bos taurus and Bos indicus (amino acid  
 XX position 63-68). This motif is capable of mimicking a fragment of the  
 XX GLUT2 protein found in insulin producing cells of the pancreas. There is  
 XX a known correlation between exposure to cow's milk and the development  
 XX of insulin-dependent diabetes which could possibly be linked to this  
 XX molecular mimicry. Dietary or pharmaceutical products derived from milk  
 XX substantially free of non-human beta casein or containing modified  
 XX beta-casein without this motif could be used in diets for the prevention  
 XX of insulin dependent diabetes particularly during early infancy.

SQ Sequence 5 AA;

AAW31288 Length: 5 March 3, 2003 11:28 Type: P Check: 1154  
 Initial Score = 5 Optimized Score = 5 Significance = -0.53  
 Residue Identity = 100% Matches = 5 Mismatches = 0  
 Gaps = 0 Conservative Substitutions = 0

X 10  
 SLVYPPFGPIP  
 |||||  
 PGP  
 X X

11. US-09-095-639A-4 (1-12)  
 p02662 Alpha-SI casein precursor.

TOIG of: p02662 check: 2471 from: 1 to: 214

ID CASL\_BOVIN STANDARD; PRT; 214 AA.  
 AC P02662; Q28048;  
 DT 21-JUL-1986 (Rel. 01, Created)  
 DT 01-NOV-1990 (Rel. 16, Last sequence update)  
 DT 01-MAR-2002 (Rel. 41, Last annotation update)  
 DE Alpha-SI casein precursor.  
 GN CSNLSI.  
 OS Bos taurus (Bovine).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;  
 OC Bovidae; Bovinae; Bos.  
 OC NCBI\_TaxID=9913;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=84221403; PubMed=6328443;  
 RA Stewart A.F., Willis I.M., Mackinlay A.G.;  
 RT "Nucleotide sequences of bovine alpha SI- and kappa-casein cDNAs";  
 RL Nucleic Acids Res. 12:3895-3907(1984).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RA Nagao M., Maki M., Sasaki R., Chiba R.;  
 RT "Isolation and sequence analysis of bovine alpha-SI-casein cDNA  
 RT clone";  
 RL Agric. Biol. Chem. 48:1663-1667(1984).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=87049835; PubMed=3022833;  
 RA Gorodetskii S.I., Zakhar'ev V.M., Kyarshulite D.R., Kapelinskaya T.V.,  
 RA Skryabin K.G.;  
 RT "cDNA of cattle alpha SI-casein: cloning and nucleotide sequence";  
 RL Biokhimiia 51:1641-1648(1986).  
 RN [4]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=92051301; PubMed=1658736;  
 RA Koczan D., Hobom G., Seyfert H.M.;  
 RT "Genomic organization of the bovine alpha-SI casein gene";  
 RL Nucleic Acids Res. 19:5591-5596(1991).  
 RN [5]  
 RP SEQUENCE OF 55-130 FROM N.A.  
 RX MEDLINE=83182023; PubMed=6897774;  
 RA Willis I.M., Stewart A.F., Caputo A., Thompson A.R., McKinlay A.G.;  
 RT "Construction and identification by partial nucleotide sequence  
 RT analysis of bovine casein and beta-lactoglobulin cDNA clones";  
 RL DNA 1:375-386(1982).  
 RN [6]  
 RP SEQUENCE OF 122-214 FROM N.A.  
 RX MEDLINE=85178933; PubMed=3838718;  
 RA Kyarshulite D.R., Zakhar'ev V.M., Gorodetskii S.I.;  
 RT "Nucleotide sequence of the 3'-nontranslated region of the mRNA of  
 RT alpha SI-casein in cows";  
 RL Dokl. Akad. Nauk SSSR 280:1433-1437(1985).  
 RN [7]  
 RP SEQUENCE OF 164-214 FROM N.A.  
 RX MEDLINE=94154154; PubMed=1343827;  
 RA Chen R., Wang B., Zhang Y., Liu W., Zhang J., Lao W.;

Mon Mar 3 11:50:09 2003

"Cloning, mapping, and sequencing of 3' and its flanking region of bovine alpha-s1 casein gene.";  
Chin. J. Biotechnol. 8:235-245(1992).

[8] SEQUENCE OF 16-214 (VARIANT B).  
MEDLINE=72063417; PubMed=4331376;  
Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
"Primary structure of bovine alpha-s1 casein. Complete sequence.";  
Eur. J. Biochem. 23:41-51(1971).

[9] REVISIONS TO 74 AND 92-93 (VARIANTS A; B; C AND D).  
MEDLINE=74082545; PubMed=4797901;  
Mercier J.-C., Grosclaude F., Ribadeau-Dumas B.;  
"Primary structure of alpha casein and of bovine beta casein.  
Correction.";  
Eur. J. Biochem. 40:323-323(1973).

[10] SEQUENCE (VARIANT D).  
MEDLINE=72214259; PubMed=5064450;  
Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
"Characterization of genetic variants of alpha-s1 and beta bovine  
caseins.";  
Eur. J. Biochem. 26:328-337(1972).

[11] SEQUENCE OF 23-49 (VARIANT A).  
Grosclaude F., Mahe M.-F., Mercier J.-C., Ribadeau-Dumas B.;  
"Localization in the N-terminal part of bovine casein alpha-s1 of a  
13 amino-acid deletion that differentiates variant A from variants B  
and C.";  
FEBS Lett. 11:109-112(1970).

[12] SEQUENCE OF 205-214 (VARIANT C).  
Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
"On the localization in the C-terminal sequence of bovine casein  
alpha-s1 of a Glu/Gly substitution that differentiates the genetic  
variants B and C.";  
C. R. Acad. Sci., D, Sci. Nat. 268:3133-3136(1970).

[13] REVISION (VARIANT C).  
Grosclaude F., Mercier J.-C., Ribadeau-Dumas B.;  
"FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT  
CALCIUM PHOSPHATE."  
CELLULAR LOCATION: Extracellular.

- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.  
- MISCELLANEOUS: THE B VARIANT SEQUENCE IS SHOWN.  
- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.  
- DATABASE: NAME=worthington enzyme manual;  
WWW="http://www.worthington-biochem.com/manual/C/CASA.html".  
- DATABASE: NAME=Protein Spotlight;  
NOTE=Issue 16 of November 2001;  
WWW="http://www.expasy.org/spotlight/articles/sptlt016.html".

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EMBL; X00564; CAB57792.1; -  
EMBL; M33123; AAA30428.1; -  
EMBL; M38641; AAA30429.1; -  
EMBL; X59856; CAA42516.1; -  
EMBL; K01084; AAA30478.1; -  
EMBL; M38658; AAA62707.1; -  
EMBL; S72388; AAD14039.1; -  
PIR; A03106; KAPOSB.  
PIR; A23071; A23071.  
PIR; S02202; S02202.  
PIR; S22575; S22575.  
InterPro; IPR001588; Casein.

DR PFam; PF00363; caseins: 1.  
DR PROSITE; PS00306; CASEIN.ALPHA.BETA: 1.  
KW Milk; Phosphorylation; Signal; Repeat.  
FT SIGNAL 1 15  
FT CHAIN 16 214 ALPHA-S1 CASEIN.  
FT MOD\_RES 61 61 PHOSPHORYLATION.  
FT MOD\_RES 63 63 PHOSPHORYLATION.  
FT MOD\_RES 68 68 PHOSPHORYLATION (IN VARIANT D).  
FT MOD\_RES 79 79 PHOSPHORYLATION.  
FT MOD\_RES 81 81 PHOSPHORYLATION.  
FT MOD\_RES 82 82 PHOSPHORYLATION.  
FT MOD\_RES 83 83 PHOSPHORYLATION.  
FT MOD\_RES 90 90 PHOSPHORYLATION.  
FT MOD\_RES 130 130 PHOSPHORYLATION.  
FT REPEAT 125 140  
FT VARIAT 29 41 MISSING (IN VARIANT A).  
FT VARIAT 68 68 A -> T (IN VARIANT D).  
FT VARIAT 207 207 E -> G (IN VARIANT C).  
FT CONFLICT 42 42 P -> L (IN REF. 3).  
FT CONFLICT 50 50 E -> Q (IN REF. 4 AND 11).  
FT CONFLICT 95 95 H -> Q (IN REF. 5).  
FT CONFLICT 143 143 H -> D (IN REF. 3).  
FT CONFLICT 203 203 S -> L (IN REF. 6).  
FT CONFLICT 211 212 NP -> IS (IN REF. 3).  
FT CONFLICT 214 214 MISSING (IN VARIANT A).  
SQ SEQUENCE 214 AA; 24529 MW; F066B5C8AE55828B CRC64;

P02662 Length: 214 February 28, 2003 14:33 Type: P Check: 2471 ..  
Initial Score = 5 Optimized Score = 7 Significance = -0.53  
Residue Identity = 25% Matches = 3 Mismatches = 8  
Gaps = 0 Conservative Substitutions = 1

X 10 X  
SLVYFPFGPIPN  
| | |  
QKEPMIGVNOELAYFPPELFRQYQLDAYPSG  
.150 X 160 170

12. US-09-095-639a-4 (1-12)  
W31294 Bovine beta casein immunogenic peptide motif 2.

ID W31294 standard; peptide; 4 AA.  
AC W31294;  
DT 05-NAR-1998 (first entry)  
DE Bovine beta casein immunogenic peptide motif 2.  
KW Beta-casein; immunogenic; molecular mimicry; cow;  
OS milk product; insulin-dependent diabetes; GLUT2; diet.  
OS Bos taurus.  
PN WO9724371-A1.  
PD 10-JUL-1997.  
PF 27-DEC-1996; E05846.  
PR 27-DEC-1995; IT-RM0850.  
PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
PA (MIDI-) MIDIA LTD.  
PI Pozzilli P;  
DR WPI; 97-363622/33.  
PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
PT food or pharmaceutical products for prevention of insulin dependent  
PT diabetes, particularly in early infancy  
PT Claim 10; Page 6; 34pp; English.  
PS This sequence represents an immunogenic peptide motif found in bovine  
CC beta casein. This motif is capable of mimicking a fragment of the  
CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
CC a known correlation between exposure to cow's milk and the development of  
CC insulin-dependent diabetes which could possibly be linked to this  
CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
CC substantially free of non-human beta casein or containing modified  
CC beta-casein without this motif could be used in diets for the prevention  
CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 4 AA; 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 0 H;

SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq  
Initial Score = 4 Optimized Score = -0.80  
Residue Identity = 100% Matches = 4 Mismatches = 0  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYPPFGPIP  
||||  
GPPI  
X X

13. US-09-095-639A-4 (1-12)  
aaw31294 Bovine beta casein immunogenic peptide motif 2.

TOIG of: aaw31294 check: 770 from: 1 to: 4

AAW31294 standard; peptide: 4 AA.

AAW31294;

DT 05-MAR-1998 (first entry)

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

DE food or pharmaceutical products for prevention of insulin dependent

DE diabetes, particularly in early infancy

DE Claim 5; Page 3; 34pp; English.

CC This sequence represents an immunogenic peptide motif from the A1

CC variant of beta-casein which is capable of mimicking a fragment of the

CC GLUT2 protein found in insulin producing cells of the pancreas. There is

CC a known correlation between exposure to cow's milk and the development of

CC insulin-dependent diabetes which could possibly be linked to this

CC molecular mimicry. Dietary or pharmaceutical products derived from milk

CC substantially free of non-human beta casein or containing modified

CC beta-casein without this motif could be used in diets for the prevention

CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 4 AA;

XX Initial Score = 4 Optimized Score = -0.80

XX Residue Identity = 100% Matches = 4 Mismatches = 0

XX Gaps = 0 Conservative Substitutions = 0

XX AAW31294 Length: 4 March 3, 2003 11:28 Type: P Check: 770 ..

XX Initial Score = 4 Optimized Score = -0.80

XX Residue Identity = 100% Matches = 4 Mismatches = 0

XX Gaps = 0 Conservative Substitutions = 0

XX AAW31294

XX DT 05-MAR-1998 (first entry)

XX Bovine beta casein immunogenic peptide motif.

XX A1 variant beta casein; immunogenic; molecular mimicry; cow;

XX milk product; insulin-dependent diabetes; GLUT2; diet.

XX Bos taurus.

XX WO9724371-A1.

XX PD 10-JUL-1997.

||||  
GPPI  
X X

14. US-09-095-639A-4 (1-12)  
w31287 Bovine beta casein variant A1 immunogenic peptide

ID W31287 standard; peptide: 5 AA.

AC W31287;

DT 05-MAR-1998 (first entry)

DE Bovine beta casein variant A1 immunogenic peptide motif.

KW A1 variant beta casein; immunogenic; molecular mimicry; cow;

KW milk product; insulin-dependent diabetes; GLUT2; diet.

OS Bos taurus.

PN WO9724371-A1.

PD 10-JUL-1997.

PF 27-DEC-1996; E05846.

PR 27-DEC-1996; IT-RM0850.

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

PA (MIDI-) MIDIA LTD.

PI Pozzilli P;

DR WPI; 97-363622/33.

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

PT food or pharmaceutical products for prevention of insulin dependent

PT diabetes, particularly in early infancy

PT Claim 5; Page 3; 34pp; English.

CC This sequence represents an immunogenic peptide motif from the A1

CC variant of beta-casein which is capable of mimicking a fragment of the

CC GLUT2 protein found in insulin producing cells of the pancreas. There is

CC a known correlation between exposure to cow's milk and the development of

CC insulin-dependent diabetes which could possibly be linked to this

CC molecular mimicry. Dietary or pharmaceutical products derived from milk

CC substantially free of non-human beta casein or containing modified

CC beta-casein without this motif could be used in diets for the prevention

CC of insulin dependent diabetes particularly during early infancy.

SQ Sequence 5 AA;

SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;

SQ 1 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 0 Y; 0 V;

CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 4 Optimized Score = -0.80

Residue Identity = 80% Matches = 4 Mismatches = 1

Gaps = 0 Conservative Substitutions = 0

SLVYPPFGPIP  
||||  
GPPI  
X X

15. US-09-095-639A-4 (1-12)  
aaw31287 Bovine beta casein variant A1 immunogenic peptide

TOIG of: aaw31287 check: 1114 from: 1 to: 5

ID AAW31287 standard; peptide: 5 AA.

XX AAW31287;

XX AAW31287;

XX DT 05-MAR-1998 (first entry)

XX Bovine beta casein variant A1 immunogenic peptide motif.

XX A1 variant beta casein; immunogenic; molecular mimicry; cow;

XX milk product; insulin-dependent diabetes; GLUT2; diet.

XX Bos taurus.

XX WO9724371-A1.

XX PD 10-JUL-1997.

XX 27-DEC-1996; 96WO-EP05846.  
 XX 27-DEC-1995; 95IT-ORM0850.  
 XX (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.  
 XX Pozzilli P;  
 PI WPI; 1997-363622/33.  
 DR Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 XX Claim 5; Page 3; 34pp; English.  
 XX This sequence represents an immunogenic peptide motif from the A1  
 CC variant of beta-casein which is capable of mimicking a fragment of the  
 CC GLUT2 protein found in insulin producing cells of the pancreas. There is  
 CC a known correlation between exposure to cow's milk and the development of  
 CC insulin-dependent diabetes which could possibly be linked to this  
 CC molecular mimicry. Dietary or pharmaceutical products derived from milk  
 CC substantially free of non-human beta casein or containing modified  
 CC beta-casein without this motif could be used in diets for the prevention  
 CC of insulin dependent diabetes particularly during early infancy.  
 XX Sequence 5 AA;

AAW31287 Length: 5 March 3, 2003 11:29 Type: P Check: 1114 ..  
 Initial Score = 4 Optimized Score = 4 Significance = -0.80  
 Residue Identity = 80% Matches = 4 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

X 10  
 SLVYFPFGPIP  
 ||||  
 GPIH  
 X X

16. US-09-095-639A-4 (1-12)  
 R37103 Bovine milk beta-casein enzymatic fragment.

ID R37103 standard; peptide; 7 AA.  
 AC R37103;  
 KW 21-MAY-1995 (first entry)  
 KW Bovine milk beta-casein enzymatic fragment.  
 KW Beta-casein; enzymatic hydrolysate; cosmetics; skin disorders;  
 KW wrinkles.  
 OS Bos Taurus.  
 PN J06166615-A.  
 PD 14-JUN-1994.  
 PF 01-DEC-1992; 321624.  
 PR 01-DEC-1992; JP-321624.  
 PA (FOKK) POLA CHEM IND INC.  
 DR WPI; 94-230615/28.  
 PT Cosmetics for treating skin disorders and wrinkles - containing  
 PT enzymatic hydrolysate of human or bovine milk beta-casein  
 PS Claim 2; Page 2; 7pp; Japanese.  
 CC The invention relates to cosmetics containing human or bovine milk  
 CC beta-casein enzymatic hydrolysate. The cosmetics are used for  
 CC improving skin disorders and/or wrinkles. They are more effective  
 CC than previously used polysaccharides, sugar alcohols, glycerol,  
 CC glycols, etc.  
 CC The present sequence is one component of the bovine milk beta-casein  
 CC enzymatic hydrolysate.  
 SQ Sequence 7 AA;  
 SQ 1 A; 1 R; 0 N; 0 D; 0 B; 0 C; 1 Q; 0 E; 0 Z; 0 G; 0 H;  
 SQ 0 I; 0 L; 0 K; 0 M; 0 F; 2 P; 0 S; 0 T; 0 W; 1 Y; 1 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:04-PST using FindSeq

Initial Score = 4 Optimized Score = 4 Significance = -0.80  
 Residue Identity = 28% Matches = 2 Mismatches = 4  
 Gaps = 0 Conservative Substitutions = 1

X 10  
 SLVYFPFGPIP  
 ||||  
 AVYFQR  
 X X

17. US-09-095-639A-4 (1-12)  
 W31293 Bovine beta casein immunogenic peptide motif 1.

ID W31293 standard; peptide; 4 AA.

AC W31293;  
 DT 05-MAR-1998 (first entry)  
 DE Beta casein immunogenic peptide motif 1.  
 KW Beta casein; immunogenic; molecular mimicry; cow;  
 KW milk product; insulin-dependent diabetes; GLUT2; diet.  
 OS Bos taurus.  
 PN WO9724371-A1.  
 PD 10-JUL-1997.  
 PF 27-DEC-1996; E05846.  
 PR 27-DEC-1995; IT-RM0850.  
 PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.  
 PA (MIDI-) MIDIA LTD.  
 PI Pozzilli P;  
 DR WPI; 97-363622/33.  
 PT Beta-casein or fragments not showing mimicry with GLUT2 - used in  
 PT food or pharmaceutical products for prevention of insulin dependent  
 PT diabetes, particularly in early infancy  
 PS Claim 10; Page 6; 34pp; English.  
 CC This sequence represents an immunogenic peptide motif of beta-casein  
 CC which is capable of mimicking a fragment of the GLUT2 protein found in  
 CC insulin producing cells of the pancreas. There is a known correlation  
 CC between exposure to cow's milk and the development of insulin-dependent  
 CC diabetes which could possibly be linked to this molecular mimicry.  
 CC Dietary or pharmaceutical products derived from milk substantially free  
 CC of non-human beta casein or containing modified beta-casein without this  
 CC motif could be used in diets for the prevention of insulin dependent  
 CC diabetes particularly during early infancy.  
 SQ Sequence 4 AA;  
 SQ 0 A; 0 R; 0 N; 0 D; 0 B; 0 C; 0 Q; 0 E; 0 Z; 1 G; 1 H;  
 SQ 1 I; 0 L; 0 K; 0 M; 0 F; 1 P; 0 S; 0 T; 0 W; 0 Y; 0 V;  
 CC Retrieved by bobryen on Thu 27 Feb 103 16:22:07-PST using FindSeq

Initial Score = 3 Optimized Score = 3 Significance = -1.06  
 Residue Identity = 75% Matches = 3 Mismatches = 1  
 Gaps = 0 Conservative Substitutions = 0

10  
 SLVYFPFGPIP  
 ||||  
 GPIH  
 X X

18. US-09-095-639A-4 (1-12)  
 aaw31293 Bovine beta casein immunogenic peptide motif 1.

TOIG of: aaw31293 check: 738 from: 1 to: 4

ID AAW31293 standard; peptide; 4 AA.

AC AAW31293;  
 XX 05-MAR-1998 (first entry)

XX Bovine beta casein immunogenic peptide motif 1.  
 XX Beta casein; immunogenic; molecular mimicry; cow;  
 XX

KW milk product; insulin-dependent diabetes; GLUT2; diet.

XX

OS

XX

PN W09724371-A1.

XX

PD 10-JUL-1997.

XX

PF 27-DEC-1996; 96WO-EP05846.

XX

PR 27-DEC-1995; 95IT-ORM0850.

XX

PA (BIOS-) BIOSISTEMA DI SARAPANI & C SAS PIER LUIG.

XX (MIDI-) MIDIA LTD.

XX

PI Pozzilli P;

XX

DR WPI; 1997-363622/33.

XX

PT Beta-casein or fragments not showing mimicry with GLUT2 - used in

XX food or pharmaceutical products for prevention of insulin dependent

PS diabetes, particularly in early infancy

XX Claim 10; Page 6; 34pp; English.

CC This sequence represents an immunogenic peptide motif of beta-casein  
CC which is capable of mimicking a fragment of the GLUT2 protein found in  
CC insulin producing cells of the pancreas. There is a known correlation  
CC between exposure to cow's milk and the development of insulin-dependent  
CC diabetes which could possibly be linked to this molecular mimicry.

CC Dietary or pharmaceutical products derived from milk substantially free  
CC of non-human beta casein or containing modified beta-casein without this  
CC motif could be used in diets for the prevention of insulin dependent  
CC diabetes particularly during early infancy.

XX Sequence 4 AA;

AAW31293 Length: 4 March 3, 2003 11:29 Type: P Check: 738 ..

Initial Score = 3 Optimized Score = -1.06  
Residue Identity = 75% Matches = 3 Mismatches = 1  
Gaps = 0 Conservative Substitutions = 0

10  
SLVYFPFGPIPN  
|||  
GPIH  
X X

